VOL. XXXVIII. JULY, 1907. NO. 1.

AMERICAN

CHEMICAL JOURNAL

ON THE CONSTITUTION OF PHENYLURAZOLE, III: A CONTRIBUTION TO THE STUDY OF TAUTOMERISM.

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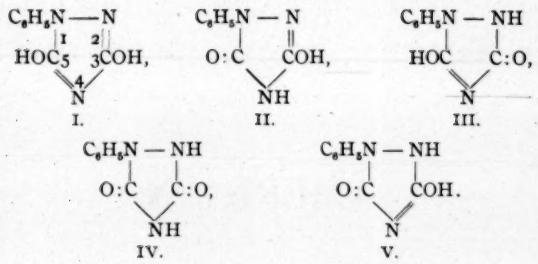
(TENTH COMMUNICATION ON THE URAZOLES.)[1]

(The writer is indebted to the Carnegie Institution of Washington for aid in this work.)

Phenylurazole and 1-phenyl-3-thiourazole and their derivatives belong to the class of substances known as tautomeric compounds. Furthermore, they are amphoteric compounds because they have both basic and acid properties. The acid characteristics, however, are decidedly predominant. In studying the constitution of these substances the following 5 formulæ must be considered:

[1] THIS JOURNAL, **27**, 118; **31**, 185; **33**, 606; **37**, 71, 361. Ber. d. chem. Ges., **35**, 553; **36**, 3139; **37**, 184, 618.



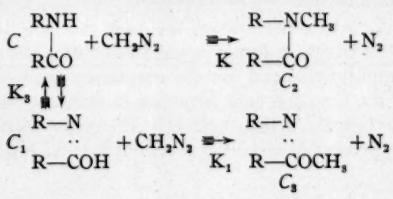
I. II. III. IV. V.

In order to study the equilibrium phenomena of the tautomeric amide groups of phenylurazole and the other urazoles, the study of the action of diazomethane on these compounds was undertaken. In phenylurazole is the 2,3 amide group a ketone, —NHCO—, or an enol, —N:C(OH)—, or a mixture of the two in equilibrium? Is the 4,5-amide group present only in 1 form or in 2 forms in equilibrium? Obviously, to secure light on this question it would be necessary to bring phenylurazole and other urazoles into reaction with some reagent that would act readily with both keto and enol forms under conditions which would, as far as possible, exclude the possibility of changing the ratio of the amounts of the 2 tautomeric forms or causing the rearrangement of either one of the derivatives into another. Diazomethane[1] seems to be a reagent admirably suited to this purpose. It has been proved that diazomethane reacts very readily with substances known to have the keto and enol structure, and it has further been shown that the methyl derivatives of phenylurazole do not rearrange into each other under the conditions of the experiments. When phenylurazole is treated, in ether, with an excess of diazomethane nearly pure 1-phenyl-3-methoxy-4-methylurazole is formed. There are present, however, traces of other dimethyl derivatives not yet identified. When phenylurazole is treated with only 1 molecule of diazomethane, about 95 per cent of 1-phenyl-3-methoxyurazole and 5 per cent of 1-phenyl-2-methylurazole are formed. These reac-

[1] Acree: Ber. d. chem. Ges., **36**, 3139. Bailey and Acree: *Ibid.*, **33**, 1529. v. Pechmann: *Ibid.*, **27**, 1888; **28**, 855, 1624; **29**, 2391; **30**, 646, *et seq.* Wegscheider: Monats. Chem., **24**, 364.

tions, then, make it appear probable that there is equilibrium between the enol and keto forms of the 2,3-amide group in phenylurazole with the enol form in great excess. But how does the 4,5-amide group react towards diazomethane? When 1-phenyl-3-methoxyurazole, 1-phenyl-3-ethoxyurazole, 1-phenyl-2-acetylurazole, or 1-phenyl-3-thiomethylurazole is treated with diazomethane the corresponding 4-methyl derivatives—that is, 1-phenyl-3-methoxy-4-methylurazole, 1-phenyl-3-ethoxy-4-methylurazole, etc., are formed nearly to the exclusion of the 5-methoxy derivatives—that is, 1-phenyl-3-methoxy-5-methoxyurazole, 1-phenyl-3-ethoxy-5-methoxyurazole, etc. These results, then, make it appear probable that the 4,5-amide group exists in 2 tautomeric forms in equilibrium, just as does the 2,3-amide group, but with the keto form in preponderance. The reactions, then, with diazomethane seem to prove that the 2,3-amide group of phenylurazole exists in ether almost entirely as enol form, but the 4,5-amide group is almost entirely a ketone, and phenylurazole exists in ether solution nearly completely in form (II.) in equilibrium with very small amounts of the other tautomeric forms.

But this evidence is certainly only qualitative, as a general discussion of such tautomeric reactions will show. It is perfectly obvious that such reactions as the above do not give us decisive evidence in regard to the relative amounts of the enol and keto forms in any given amide group (or other tautomeric group) in which the change from one tautomeric form to the other is very rapid in comparison with the reactions between the 2 forms and the alkylating (or acylating, etc.) reagents. To illustrate graphically, in 1 liter of solution, let C and C_1 be the number of gram-molecules of the 2 tauto-



meric forms, in constant equilibrium, reacting with $C + C_1$ gram-molecules of diazomethane (or other reagents) and forming C_2 and C_3 gram-molecules of the stable isomeric derivatives in the time interval T. If neither C_2 nor C_3 rearranges into the other and if C_2 and C_3 are formed from C and C_1, respectively, by reactions of the second order, it is evident that the velocity with which C_2 and C_3 are formed is a function of the total concentration of the tautomeric substance and of the concentration of the diazomethane (or other reagent). At the end of the time T the concentration of the tautomeric substance, and also of the diazomethane, is $(C + C_1 - C_2 - C_3)$. The theory of side reactions gives us the following equations to express the course of the reactions in question:

$$\frac{dC_2}{dT} = K(C + C_1 - C_2 - C_3)^2. \qquad (1)$$

$$\frac{dC_3}{dT} = K_1(C + C_1 - C_2 - C_3)^2. \qquad (2)$$

Dividing (1) by (2) we get

$$\frac{dC_2}{dC_3} = \frac{K}{K_1} = K^1. \qquad (3)$$

Integrating (3) we get

$$C_2 = K^1C_3 + K^{II}. \qquad (4)$$

If, in (4), $C_2 = o$, then $C_3 = o$, and $K^{II} = o$, and we get from (3)

$$\frac{C_2}{C_3} = K^1. \qquad (5)$$

That is, the ratio of the amounts of the 2 esters formed during various time intervals is a constant.

If we take into consideration the fact that the tautomeric compound exists in 2 forms in constant ratio, the equations must be slightly changed but the conclusion arrived at is the same. If the keto and enol forms are in constant equilibrium, that is, if $C = K_2C_1$, then evidently the concentration of the keto form present at any moment is not $(C + C_1 - C_2 - C_3)$ but

$\frac{K_3}{1+K_3}(C + C_1—C_2—C_3)$, and the concentration of the enol tautomer is $\frac{1}{1+K_3}(C + C_1—C_2—C_3)$. Equations (1) and (2) above then become

$$\frac{dC_2}{dT}=\frac{KK_3}{1+K_3}(C+C_1—C_2—C_3)^2, \qquad (6)$$

and

$$\frac{dC_3}{dT}=\frac{K_1}{1+K_3}(C+C_1—C_2—C_3)^2. \qquad (7)$$

By dividing (6) by (7) we get equation (8),

$$\frac{dC_2}{dC_3}=\frac{KK_3}{K_1}=K^{III}, \qquad (8)$$

which by integration as in (4) and (5) gives (9),

$$\frac{C_2}{C_3}=\frac{KK_3}{K_1}=K^{III}, \qquad (9)$$

which has the same form as (5). Since the ratio $\frac{C_2}{C_3}$ can be measured experimentally, it is evident that the value of K^{III} can be determined.

By addition (6) and (7) give

$$\frac{d(C_2+C_3)}{dT}=\frac{KK_3+K_1}{1+K_3}(C+C_1—C_2—C_3)^2= K^{IV}(C+C_1—C_2—C_3)^2, \qquad (10)$$

which by integration gives

$$\frac{C_2+C_3}{T(C+C_1—C_2—C_3)}=\frac{(C+C_1)(KK_3+K_1)}{1+K_3}=K^{IV}(C+C_1). \qquad (11)$$

Since T and $C_2 + C_3$ can be measured experimentally and $C+C_1$ is known, it is evident that the value of $\frac{KK_3+K_1}{1+K_3}$ or K^{IV} can be determined.

But in the 2 equations, $\frac{KK_3}{K_1}=K^{III}$ and $\frac{KK_3+K_1}{1+K_3}=K^{IV}$

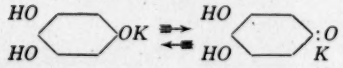
there are 3 unknown quantities; it is impossible to determine the value of K, K_1 or K_2 from these 2 equations alone. Unless by some conductivity, spectroscopic, or other means we can determine the value of one of these constants, we cannot hope to learn the quantitative relations of these tautomeric compounds in which the change from one form to another is very rapid. The above ideas have received[1] quantitative confirmation in the study of the reactions between alkyl halides and the salts of 1-phenyl-4-methylurazole and 1-phenyl-3-thiourazole. It has been found that the salts exist in enol and keto forms in equilibrium, and that the enol and keto anions, E and K, react with the alkyl halides and form O- and N-esters. The discussion holds for reactions which involve the enol and keto anions just as surely as it does for the molecular tautomers.

$$\underset{K}{\overset{+}{\mathrm{Na}}+\overset{-}{\mathrm{N}}(\mathrm{R})\mathrm{COR}} \rightleftarrows \mathrm{NaN(R)COR} \rightleftarrows$$

$$\underset{E}{\mathrm{RN:C(R)ONa}} \rightleftarrows \mathrm{RN:C(R)}\overset{-}{\mathrm{O}}+\overset{+}{\mathrm{Na}}.$$

In all of the alkylation reactions of the following and similar salts in which two products are formed, it is believed (1) that there may be two salts in equilibrium somewhat as expressed below, or (2) that one of the alkyl derivatives is formed from the other. We shall study the reactions of such tautomeric salts and acids in the light of this hypothesis.

$$KNC \rightleftarrows KCN$$
$$KONO \rightleftarrows KNO_2$$
$$KOCN \rightleftarrows KNCO$$
$$KOCR:S \rightleftarrows KSCR:O$$
$$(KO)_2S:O \rightleftarrows KSO_2OK$$



[1] Acree: This Journal, **37**, 71.

But in the case of phenylurazole we have fairly good evidence on the value of the ratio $\frac{K}{K_1}$; that is, the relative activity of the keto and the enol forms towards diazomethane. A study of the reactions of various urazoles has shown that the imido group at —4— reacts practically as rapidly as the enol group at —3; in other words, the value of $\frac{K}{K_1}$ is nearly unity. From equation (9), then, we get another equation,

$$\frac{C_2}{C_3}=\frac{KK_3}{K_1}=K_3, \qquad (12)$$

that is, the ratio of the amounts of enol ester and keto ester formed in a given time interval T, is approximately the ratio of the amounts of the enol and keto forms of the amide group. In phenylurazole in ether solution then, since the 2,3-amide group gives 95 per cent of 1-phenyl-3-methoxyurazole and 5 per cent of 1-phenyl-2-methylurazole, this amide group is probably 95 per cent enol and 5 per cent ketone. On the other hand, the same kind of evidence shows the 4,5-amide group to be in ether solution about 95 per cent keto form and 5 per cent enol form. These figures, however, are only approximate, as the value of the ratio $K:K_1$ was not very accurately determined. This work is being carried further to secure more accurate data.

In order to simplify the following discussion of other cases we shall take the value of T to be so small that the values of C and C_1 are not appreciably diminished. Therefore, during the time interval T let $C_2 = K'C$ and $C_3 = K''C_1$. The real quantitative relations between C and C_2, C_1 and C_3, etc., would, of course, have to depend upon the differential equations given above.

Suppose that in a given amide the ratio $C:C_1 = 1:100$, and the ratio $K':K'' = 100$. It is apparent then that the ratio of the amounts of the alkyl derivatives formed, $C_2:C_3 = 1$. The ratio of the amounts of the derivatives obtained will, therefore, in such a case, give no clue to the ratio of the 2 tautomeric forms of the amide group. But if $K':K'' = 1$, in

other words, if the reactivity of both tautomeric forms towards the alkylating (or other) reagent is the same, then the ratio $C_2 : C_3$ is exactly equal to the ratio $C : C_1$ and a determination of the ratio $C_2 : C_3$ gives us the value of $C : C_1$. Our urazoles, both tautomeric forms of which react with diazomethane with about the same readiness, come under this class.

If, on the other hand, the change from one tautomeric form, C, to the other, C_1, is very slow in comparison with the speed of the alkylation reactions, and if $K' = K''$, then the ratio $C_2 : C_3$ is nearly equal to the ratio $C : C_1$. But if K' and K'' are not equal then again the ratio $C_2 : C_3$ cannot be equal to the ratio $C : C_1$.

It might be thought that if we could measure the value of K' and of K'' in similar reactions with substances known to have the constitution of C and C_1 we could obtain the value of $C : C_1$ from the value of $C_2 : C_3$. Under what conditions can the ratio $C_2 : C_3$ be approximately constant for a few time intervals T and be equal to the ratio $K'C : K''C_1$? It is evident that such can be the case (1) when the change from C to C_1, or *vice versa*, is instantaneous in comparison with the speed of the 2 alkylation reactions. When $C : C_1$ and $K' : K''$ are constant, $C_2 : C_3$ will be constant, and $C_2 : C_3 = K'C : K''C_1$. And in such a case we must know the value of $K' : K''$ in order to be able to determine the value of $C : C_1$, or *vice versa*. (2) If the change of C into C_1, or *vice versa*, is very slow in comparison with the alkylation reactions, and if $K' = K''$, then the ratio $C_2 : C_3$ will be approximately constant for a short time and will be equal to the ratio $C : C_1$.

If the ratio $C : C_1$ is changing considerably during the alkylation reaction, as one or the other form is removed the more rapidly, since $K' : K''$ is constant, $C_2 : C_3$ must change at the same rate.

It is, therefore, clear that the ratio $C_2 : C_3$ of the amounts of the stable alkyl (or other) derivatives formed from a tautomeric substance and an alkylating (or other) reagent depend upon 3 things: (1) the relative reactivity of the 2 tautomeric forms towards the other reagent; (2) the ratio between the amounts of the 2 tautomeric forms when they are in constant

equilibrium with each other; and (3) the rapidity of the change of each of these tautomeric forms into the other as the equilibrium between them is disturbed. This reaction may, in certain cases, be complicated by the rearrangement of one, or each, of the tautomeric derivatives into the other, or some other product.

Unless we know (1) and (3) from other data we cannot use the ratio of the amounts of the derivatives found to determine the ratio of the amounts of the 2 tautomeric forms. In other words, the mere fact that we get only 1 derivative from a tautomeric substance and another reagent furnishes no evidence whatever in regard to the constitution of the tautomeric substance. A tautomeric substance having nearly completely the enol form could give completely a ketone derivative if the enol form does not react with the reagent, but the ketone form does enter into such a reaction.

It is clear then that we cannot use such reagents as phenylhydrazine, phenylisocyanate, etc., to determine the constitution of such things as acetoacetic ester, because we do not know the relative activity of the enol and keto forms towards these reagents, the ratio of the amounts of the 2 tautomeric forms, or the rapidity of change of one tautomer into the other. At best, we know only that ketones do react with phenylhydrazine, probably first by addition,[1] and also that acids[2] (enols) condense with hydrazines, amines, etc., and form hydrazides and amides. The same hydrazide of acetoacetic ester could be formed from either the keto or enol form by reactions perfectly analogous to others well known.

$$CH_3COCH_2COOR + NH_2NHC_6H_5 \rightarrow CH_3C(OH)(NHNHC_6H_5)CH_2COOR \rightarrow CH_3C(NHNHC_6H_5):CHCOOR + H_2O;$$

$$CH_3C(OH):CHCOOR + NH_2NHC_6H_5 \rightarrow CH_3C(NHNHC_6H_5):CHCOOR + H_2O.$$

[1] Nef: Ann. Chem. (Liebig), **270**, 289, 333. Städeler: *Ibid.*, **106**, 253. Schiff: Ber. d. chem. Ges., **10**, 165. Wislicenus and Scheidt: *Ibid.*, **24**, 3006.

[2] Tingle: THIS JOURNAL, **19**, 408. Tingle and Hoffman: *Ibid.*, **34**, 1227. Tingle and Robinson: *Ibid.*, **36**, 234.

Goldschmidt[1] thought that phenylisocyanate should react readily only with the enol group of acetoacetic ester, but Dieckmann[2] and Michael[3] proved afterwards that the reaction product from acetoacetic ester, or its sodium salt, is really a carbon derivative, acetylmalonic acid ester anilide.

In order to study this problem of tautomerism with any success we must use quantitative methods to study (1), (2) and (3) with as many tautomeric substances (including their salts) and at different temperatures, in different solvents, etc., as possible, and that is being done in this laboratory.

It was shown above and in a previous paper that the reactions of phenylurazole and 1-phenyl-3-thiourazole with diazomethane make it probable that these urazoles exist in solution nearly completely in the form (II.), in equilibrium with the other forms. It may be stated that all of the evidence secured since that time bear out this conclusion. In order to arrive at the correct mathematical expression of the relations between the ionic and molecular forms of these tautomeric compounds in various solvents,[4] in different concentrations, at different temperatures, and under various other conditions, it will evidently be necessary to know whether the equilibrium is between molecules or anions, whether both tautomeric forms give hydrogen ions, whether the ionization of each tautomeric form follows Ostwald's dilution law, or one like van't Hoff's, Rudolphi's or Storch's dilution equation, and other points which, for lack of space, cannot be discussed in this article. Will the data obtained by conductivity methods alone give us any information concerning the equilibrium conditions in a solution of any tautomeric compound?

To illustrate by one of the several different cases that would arise under the conditions spoken of above, let us assume that we are dealing with an amide whose 2 tautomeric forms give

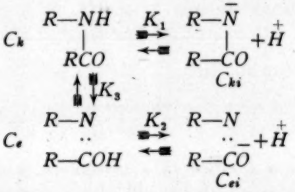
[1] Goldschmidt and Meissler: Ber. d. chem. Ges., **23**, 253.

[2] *Ibid.*, **23**, 2002.

[3] J. prakt. Chem., **35**, 451; **60**, 316. Ber. d. chem. Ges., **29**, 1794.

[4] Hantzsch and students: Ber. d. chem. Ges., **29**, 699, 2251; **32**, 607, 3066; **34**, 3142; **35**, 210, 265, 1001. Goldschmidt and Oslan: *Ibid.*, **32**, 3390. Dedichen: *Ibid.*, **29**, 1831. Trübebach: Z. physik. Chem., **16**, 708. Wood: J. Chem. Soc., **89**, 1831, 1839.

hydrogen ions in accordance with Ostwald's dilution law, and that the equilibrium is established practically instantaneously, and is between the molecular forms as in the case of Dimroth's[1] ethyl 1-phenyl-1,2,3-triazole-5-oxy-4-carboxylate.



I. In the volume of solution V let there be C_k and C_e gram molecules of the keto and enol forms, respectively, giving C_{ki} and C_{ei} gram equivalents of their respective ions. Let H gram equivalents of hydrogen ions be present, and let K_1 and K_2 be the dissociation constants of the keto and enol forms, respectively.

Let

$$C_k = K_3 C_e, \tag{1}$$

$$\frac{H \times C_{ki}}{C_k} = K_1 V, \tag{2}$$

and

$$\frac{H \times C_{ei}}{C_e} = K_2 V. \tag{3}$$

From (1) and (2) by substitution,

$$\frac{H \times C_{ki}}{C_e} = K_1 K_3 V. \tag{4}$$

From (2) and (4) by inversion and addition,

$$\frac{H \times C_{ki}}{(C_k + C_e)} = \frac{K_1 K_3 V}{1 + K_3}. \tag{5}$$

From (1), (2) and (3) by substitution,

[1] Ann. Chem. (Liebig), **335**, 1; **338**, 143.

$$C_{ki} = \frac{K_1 K_3 C_{ei}}{K_2}. \qquad (6)$$

From (5) and (6) by substitution,

$$\frac{H \times C_{ei}}{(C_k + C_e)} = \frac{K_2 V}{1 + K_3}. \qquad (7)$$

From (5) and (7) by addition,

$$\frac{H \times (C_{ki} + C_{ei})}{(C_k + C_e)} = \frac{(K_2 + K_1 K_3) V}{1 + K_3} = KV. \qquad (8)$$

In other words, a solution of a tautomeric substance having the properties described above will give a constant according to Ostwald's dilution law. The fact that a constant is obtained by substituting the experimental data in Ostwald's dilution formula does not enable us to decide whether the tautomeric compound exists in 2 forms in equilibrium as in I., or exists as only 1 form. Phenylurazole comes under this case. The conductivity data show that phenylurazole gives a constant according to equation (8); but only by the use of chemical reactions was it possible to prove that both tautomeric forms of the 2,3-amide group are present. The value of the constant found by experiment, K, is a function of the constants of the 2 tautomeric forms, $\frac{K_1 + xK_2}{1 + x}$, as is approximately the case with isohydric mixtures of 1 volume of acetic acid and x volumes of butyric acid, or any weak acids not tautomeric or dependent on each other. The ionic velocity of C_{ki} will be the same as that of C_{ei}, or so near it, that we may take them to be the same in all these equations; this is generally the case with isomers, such as the *o*-, *m*- and *p*-toluic acids, etc. The value of the constant obtained, say by conductivity methods, gives no data in regard to the relative magnitude of K_1, K_2 and K_3, or the relative amounts of enol and keto forms, and these values must be obtained by other methods. If by another method it were found that K_3 is very small in comparison with K_1 and K_2, then $\frac{K_2 + K_1 K_3}{1 + K_3}$

would become nearly equal to K_2 or K, and the determination of the value of K by conductivity methods would be really the determination of the value of K_2. It is further evident that the above discussion can be widened to the consideration of the 2 amide groups in phenylurazole, and to the salts of all tautomeric compounds.

II. If one tautomer, say, the keto form, gives no hydrogen ions,[1] or $K_1 = 0$, and the other obeys Ostwald's dilution law, the equilibrium between the molecular forms remaining as in I, then the equations are the following:

Let

$$C_k = K_3 C_e \qquad (1)$$

and

$$\frac{H \times C_{ei}}{C_e} = K_2 V. \qquad (2)$$

Then from (1) and (2) by substitution,

$$\frac{H \times C_{ei}}{C_k} = \frac{K_2 V}{K_3}. \qquad (3)$$

Therefore, from (2) and (3) by addition

$$\frac{H \times C_{ei}}{(C_k + C_e)} = \frac{K_2 V}{1 + K_3} = KV. \qquad (4)$$

In such a case the tautomeric compound will obey Ostwald's dilution law, but the data obtained give us no information in regard to the ratio of the amounts of the enol and keto forms; that is, the relative values of K_2 and K_3. As the value of K_3 becomes smaller, and the keto form disappears, the value of K measured approaches that of the Ostwald constant, K_2, for the enol form. Phenyl-3-thiourazole comes under this last heading. Phenyl-3-thiourazole gives a constant according to equation (4), and a number of chemical reactions show the value of K_3 to be very small for the 2,3-thioamide group. This group, then, seems to exist nearly completely in the enol form.

[1] Zawidzki: Ber. d. chem. Ges., **37**, 2298. Kauffmann: *Ibid.*, **37**, 2468; Z. physik. Chem., **47**, 621. Euler: Ber. d. chem. Ges., **39**, 1607, 2265. Hantzsch and students: *Ibid.*, **38**, 210, 226, 1001, *et seq.*

III. If one tautomer, the keto form, obeys Ostwald's dilution law and the other obeys Rudolphi's dilution formula, and the equilibrium between the molecular forms is the same as in I., the equations assume the following forms. Let

$$C_k = K_3 C_e, \tag{1}$$

$$\frac{H \times C_{ki}}{C_k} = K_1 V, \tag{2}$$

and

$$\frac{H \times C_{ei}}{C_e} = K_2 \sqrt{V}. \tag{3}$$

Then from (4) .... (9) in I.,

$$\frac{H \times (C_{ki} + C_{ei})}{(C_k + C_e)} = \frac{K_1 K_3 V + K_2 \sqrt{V}}{1 + K_3}. \tag{4}$$

If C_e becomes nearly zero, then (4) approaches (5) in form.

$$\frac{H \times C_{ki}}{C_k} = K_1 V. \tag{5}$$

If C_k becomes nearly zero, then (4) approaches (6) in form.

$$\frac{H \times C_{ei}}{C_e} = K_2 \sqrt{V}. \tag{6}$$

It is evident that when the value of K_3 is near unity and K_1 and K_2 have comparable values, we cannot get a constant by substituting in (4) the data obtained by conductivity measurements. Only when C_e or C_k becomes nearly zero would we get an approximate constant, according to (5) or (6).

IV. If both tautomeric forms obey Rudolphi's dilution formula and the equilibrium between the molecular enol and keto forms is the same as in I., the equations become

$$C_k = K_3 C_e, \tag{1}$$

$$\frac{H \times C_{ki}}{C_k} = K_1 \sqrt{V}, \tag{2}$$

and

$$\frac{H \times C_{ei}}{C_e} = K_2 \sqrt{V}. \tag{3}$$

Then from (4) in III. we get

$$\frac{H\times(C_{ki}+C_{ei})}{(C_k+C_e)}=\frac{(K_2+K_1K_3)\sqrt{v}}{1+K_3}=K\sqrt{v}. \qquad (4)$$

In this case a constant will be obtained by substituting the data found in the Rudolphi formula (4), and the alkali salts of the urazoles give very good constants. The relation of the value of K to that of K_1 or K_2 will depend upon the value of K_3, and the data obtained give no information concerning the relative amounts of enol and keto forms present. The same constant would be derived even if the substance existed in only one (tautomeric) form which obeys Rudolphi's dilution formula. But it has been proved by quantitative work on the reactions between salts of 1-phenyl-4-methylurazole and alkyl halides that the salts are actually present in both enol and keto forms.

V. If the keto tautomer gives no hydrogen ions and the enol form obeys Rudolphi's dilution formula and the equilibrium is the same as in I. the equations are

$$C_k=K_3C_e, \qquad (1)$$

and

$$\frac{H\times C_{ei}}{C_e}=K_2\sqrt{v}. \qquad (2)$$

Therefore from (3) and (4), in II., we get

$$\frac{H\times C_{ei}}{C_k}=\frac{K_2\sqrt{v}}{K_3} \qquad (3)$$

and

$$\frac{H\times C_{ei}}{(C_k+C_e)}=\frac{K_2\sqrt{v}}{1+K_3}=K\sqrt{v}. \qquad (4)$$

In this case, as in II., we should obtain a constant by substituting in (4) the data obtained by experiment. As the value of K_3 approaches zero the value of K found approaches that of K_2. Unless we can obtain, by other means, the value of K_2 or K_3, the value of K in (4), as determined by conductivity methods, gives us no data in regard to the relative values of K_2 and K_3. It is evident that the salts formed by these

tautomeric acids and strong bases must probably be treated under IV. and V. Some salts may, however, ionize so little that they may be treated under I., II., or III. It will be recalled that mercuric chloride and mercuric cyanide give nearly a constant when the data showing the ionization are substituted in Ostwald's dilution formula. The per cent of ionization, as well as the per cent of hydrolysis, of each tautomeric salt in aqueous solution, will depend upon the strength of the acid and the base which forms the salt, and upon the concentration and temperature of the solution.

VI. In the equations worked out in I....V., the assumption was made that the molecular forms of the enol and keto tautomers are in equilibrium. We can readily see, however, that other cases must be considered in which the anions corresponding to the enol and keto forms are in equilibrium. Evidently, as in the cases considered above, the enol and keto forms may give constants according to Ostwald's dilution formula or Rudolphi's (van't Hoff's or Storch's) dilution formula, and all these cases must be considered. In VI. we shall assume that both enol and keto forms give ionization constants according to Ostwald's dilution formula.

Let

$$C_{ki} = K_3 C_{ei}, \tag{1}$$

$$\frac{H \times C_{ki}}{C_k} = K_1 V \tag{2}$$

and

$$\frac{H \times C_{ei}}{C_e} = K_2 V. \tag{3}$$

From (1) and (2), by substitution,

$$\frac{H \times C_{ei}}{C_k} = \frac{K_1 V}{K_3}. \tag{4}$$

Therefore, from (2) and (4), by addition,

$$\frac{H \times (C_{ki} + C_{ei})}{C_k} = \frac{(1 + K_3) K_1 V}{K_3}. \tag{5}$$

From (1) and (5), by substitution,

$$\frac{H\times(C_{kl}+C_{el})}{C_e}=(1+K_3)K_2V. \qquad (6)$$

From (5) and (6), by inversion and addition,

$$\frac{H\times(C_{kl}+C_{el})}{(C_k+C_e)}=\frac{K_1K_2(1+K_3)V}{K_1+K_2K_3}=KV. \qquad (7)$$

Evidently, then, as the value of K_3 approaches zero the value of K approaches that of K_2. As the value of K_3 approaches infinity the value of $K_1 + K_2K_3$ approaches that of K_2K_3 and the value of K approaches that of K_1. It is further evident that since the tautomeric compound gives a constant according to the Ostwald dilution formula in I. or VI., the value of this constant and the other data obtained by conductivity methods cannot give us any information as to whether the equilibrium is between the molecular enol and keto forms or between the anions from these forms. This holds also for the 2 following cases. The quantitative study of certain reactions, however, would enable us to decide whether the equilibrium is between the anions or the molecular tautomers. This has been done, for instance, in the case of the alkali salts of 1-phenyl-4-methylurazole. These salts give a constant in Rudolphi's dilution equation, and it is impossible to tell from conductivity data whether the equilibrium is in accordance with IV. or VII. But the study[1] of the reactions between these salts and alkyl halides has shown that the equilibrium is between the molecular tautomers, as in IV., and not between the anions, as in VII.

VII. Let us suppose that both tautomers ionize according to Rudolphi's dilution formula and that the anions are in equilibrium as in VI.

The equations will be identical with those in VI, with the exception that $\sqrt{V}$ must take the place of V. Equation (7) in VI. becomes

$$\frac{H\times(C_{kl}+C_{el})}{(C_k+C_e)}=\frac{K_1K_2(1+K_3)\sqrt{V}}{K_1+K_2K_3}=K\sqrt{V}. \qquad (1)$$

It is evident, then, that a constant would be obtained in

[1] Acree: THIS JOURNAL, 37, 84.

this case just as in IV. The conductivity data alone would not give any evidence as to whether the equilibrium is between the molecular enol and keto forms or between their anions, nor would the value of K, determined by this means, give any data in regard to the relative magnitude of K_1, K_2 and K_3.

VIII. Let the keto form obey Ostwald's dilution formula and the enol form obey Rudolphi's dilution formula and let the equilibrium be between the anions corresponding to the enol and keto forms.

Then

$$C_{ki} = K_3 C_{ei}, \tag{1}$$

$$\frac{H \times C_{ki}}{C_k} = K_1 V \tag{2}$$

and

$$\frac{H \times C_{ei}}{C_e} = K_2 \sqrt{V}. \tag{3}$$

Therefore, from (1) and (2), by substitution,

$$\frac{H \times C_{ei}}{C_k} = \frac{K_1 V}{K_3}. \tag{4}$$

From (2) and (4), by addition,

$$\frac{H \times (C_{ki} + C_{ei})}{C_k} = \frac{K_1 (1 + K_3) V}{K_3}. \tag{5}$$

From (1) and (3), by substitution,

$$\frac{H \times C_{ki}}{C_e} = K_2 K_3 \sqrt{V}. \tag{6}$$

From (3) and (6), by addition,

$$\frac{H \times (C_{ki} + C_{ei})}{C_e} = K_2 (1 + K_3) \sqrt{V}. \tag{7}$$

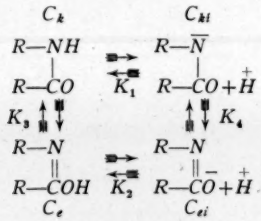
From (5) and (7), by inversion and addition,

$$\frac{H \times (C_{ki} + C_{ei})}{(C_k + C_e)} = \frac{K_1 K_2 (1 + K_3) V}{K_2 K_3 + K_1 \sqrt{V}}. \tag{8}$$

It is evident that, as in III., no constant can be obtained in (8) when K_1, K_2 and K_3 have comparable values. Further-

more, since no constant can be obtained in equation (4) in III., nor in equation (8) in VIII., when K_1, K_2 and K_3 have comparable values, it is impossible to tell by simple conductivity data when one tautomer obeys Ostwald's dilution formula and the other Rudolphi's dilution formula, whether the equilibrium is between the molecular forms of the tautomers or between their anions.

IX. It is evident that the case must be considered in which the molecular enol and keto forms are in equilibrium and at the same time the anions of the enol and keto forms are in equilibrium. We must first consider whether such relations can possibly exist, and, if so, under what conditions the molecular forms can exist in equilibrium while the anions are in equilibrium. Let the assumption be made that both tautomers obey Ostwald's dilution law. Let C_k, C_e, C_{ki} and C_{ei} be the number of gram equivalents of the keto molecular tautomer, enol molecular tautomer, keto anion, and enol anion, respectively, in the volume V of solution. Let the equilibrium constants be shown in the accompanying illustration and in the succeeding equations. Let H represent the number of gram equivalents of hydrogen ions. Let



$$C_k = K_3 C_e, \qquad (1)$$

$$C_{ki} = K_4 C_{ei}, \qquad (2)$$

$$\frac{H \times C_{ki}}{C_k} = K_1 V, \qquad (3)$$

and

$$\frac{H\times C_{ei}}{C_e}=K_2V. \qquad (4)$$

From (2) and (3), by substitution,

$$\frac{H\times C_{ei}}{C_k}=\frac{K_1V}{K_4}. \qquad (5)$$

From (3) and (5), by addition,

$$\frac{H\times(C_{ki}+C_{ei})}{C_k}=\frac{K_1V}{K_4}+K_1V=\frac{K_1(1+K_4)V}{K_4}. \qquad (6)$$

From (1) and (6), by substitution,

$$\frac{H\times(C_{ki}+C_{ei})}{K_3C_e}=\frac{K_1(1+K_4)V}{K_4} \text{ or}$$

$$\frac{H\times(C_{ki}+C_{ei})}{C_e}=\frac{K_1K_3(1+K_4)V}{K_4}. \qquad (7)$$

From (6) and (7), by inversion and addition,

$$\frac{H\times(C_{ki}+C_{ei})}{(C_k+C_e)}=\frac{K_1K_3(1+K_4)V}{K_4(1+K_3)}=K'V. \qquad (8)$$

Since K' does not involve K_2, it is evident that another solution is possible. From (1) and (4), by substitution,

$$\frac{H\times C_{ei}}{C_k}=\frac{K_2V}{K_3}. \qquad (9)$$

From (3) and (9), by addition,

$$\frac{H\times(C_{ki}+C_{ei})}{C_k}=\frac{(K_2+K_1K_3)V}{K_3}. \qquad (10)$$

From (1) and (10), by substitution,

$$\frac{H\times(C_{ki}+C_{ei})}{C_e}=(K_2+K_1K_3)V. \qquad (11)$$

From (10) and (11), by inversion and addition,

$$\frac{H\times(C_{ki}+C_{ei})}{(C_k+C_e)}=\frac{(K_2+K_1K_3)V}{(1+K_3)}=K''V. \qquad (12)$$

From (8) and (12), by comparison and identity,

$$\frac{K_3(K_1+K_1K_4)}{K_4(1+K_3)}=\frac{(K_1K_3+K_2)}{(1+K_3)} \text{ or } \frac{K_1}{K_2}=\frac{K_4}{K_3}. \qquad (13)$$

It is evident, then, that when the molecular tautomeric

forms are in equilibrium, the anions of the enol and keto forms can be in equilibrium simultaneously only when the ratio of the dissociation constant of the keto form, K_1, to that of the enol form, K_2, is equal to the ratio of the equilibrium constant for the anions, K_4, to that of the molecular forms, K_3. The fact that a constant is obtained when the experimental data are substituted in Ostwald's dilution formula, does not in the least enable us to say whether the equilibrium of the tautomeric substance coresponds to I., II., VI., or IX. Other physical-chemical methods would be needed to give decisive evidence regarding the real equilibrium conditions.

X. The next case to be considered is that which arises when both tautomers obey Rudolphi's dilution formula and the other conditions are the same as in IX. The equations are exactly like those in IX, with the exception that $\sqrt{V}$ must be substituted for V in the equations developed under IX. From (8) in IX.,

$$\frac{H\times(C_{ki}+C_{ei})}{(C_k+C_e)}=\frac{K_3(K_1+K_1K_4)\sqrt{V}}{K_4(1+K_3)}=K'\sqrt{V}. \qquad (1)$$

From (12) in IX.,

$$\frac{H\times(C_{ki}+C_{ei})}{(C_k+C_e)}=\frac{(K_2+K_1K_3)\sqrt{V}}{(1+K_3)}=K''\sqrt{V}. \qquad (2)$$

From (13) in IX.,

$$\frac{K_1}{K_2}=\frac{K_4}{K_3}. \qquad (3)$$

It is clear that the conditions of equilibrium in X. are dependent upon the same factors as in IX. The fact that a constant is obtained by substituting the experimental data in Rudolphi's dilution equation does not give us any evidence as to whether the equilibrium corresponds to IV., V., VII., or X. Other methods would have to be used to decide the question.

XI. Can the molecular enol and keto forms be in equilibrium while the anions of the enol and keto forms are in equilibrium, and simultaneously can one tautomer obey Ostwald's dilution law and the other Rudolphi's dilution formula? Can

all these conditions exist simultaneously? If not all, how many? If possible, let

$$C_h = K_3 C_e, \tag{1}$$

$$C_{hi} = K_4 C_{ei}, \tag{2}$$

$$\frac{H \times C_{hi}}{C_h} = K_1 V, \tag{3}$$

and

$$\frac{H \times C_{ei}}{C_e} = K_2 \sqrt{V}. \tag{4}$$

From (2) and (3), by substitution,

$$\frac{H \times C_{ei}}{C_h} = \frac{K_1 V}{K_4}. \tag{5}$$

From (3) and (5), by addition,

$$\frac{H \times (C_{hi} + C_{ei})}{C_h} = \frac{K_1 (1 + K_4) V}{K_4}. \tag{6}$$

From (1) and (6), by substitution,

$$\frac{H \times (C_{hi} + C_{ei})}{C_e} = \frac{K_1 K_3 (1 + K_4) V}{K_4}. \tag{7}$$

From (6) and (7), by inversion and addition,

$$\frac{H \times (C_{hi} + C_{ei})}{(C_h + C_e)} = \frac{K_1 K_3 (1 + K_4) V}{K_4 (1 + K_3)}. \tag{8}$$

As the equation (8) does not involve K_2, another solution, involving K_2, is possible.

From (1) and (4), by substitution,

$$\frac{H \times C_{ei}}{C_h} = \frac{K_2 \sqrt{V}}{K_3}. \tag{9}$$

From (3) and (9), by addition,

$$\frac{H \times (C_{hi} + C_{ei})}{C_h} = \frac{K_1 K_3 V + K_2 \sqrt{V}}{K_3}. \tag{10}$$

From (1) and (10), by substitution,

$$\frac{H \times (C_{hi} + C_{ei})}{C_e} = K_1 K_3 V + K_2 \sqrt{V}. \tag{11}$$

From (10) and (11), by inversion and addition,

$$\frac{H\times(C_{hl}+C_{el})}{(C_h+C_e)}=\frac{K_1K_3V+K_2\sqrt{V}}{1+K_3}. \qquad (12)$$

It is apparent that from equation (8) we should obtain a constant by substituting the proper experimental data in Ostwald's dilution formula, whereas from equation (12) it seems that no such constant can be derived. This apparent contradiction disappears upon closer inspection of the development of equations (8) and (12). In equation (8) the factor K_3 does not enter; in other words, no assumption is made that C_e is in equilibrium with C_{el} at all, much less according to equation (4). This is a new set of conditions, to be added to I., II., VI., and IX., under which a constant can be obtained from Ostwald's dilution law with such tautomeric compounds. Similarly, from equations (1), (2) and (4) another equation, similar to (8), but involving K_2 instead of K_1 and $\sqrt{V}$ instead of V, can be developed. The equation is

$$\frac{H\times(C_{hl}+C_{el})}{(C_h+C_e)}=\frac{K_2(1+K_4)\sqrt{V}}{1+K_3}=K''\sqrt{V}. \qquad (13)$$

These are a new set of equilibrium conditions, to be added to IV., V., VII. and X., under which a constant can be obtained from Rudolphi's dilution equation, with a tautomeric substance.

In equation (12) the factor K_4 does not enter; in other words, no assumption is made that the anions C_{hl} and C_{el} are in equilibrium. In equation (12), then, the conditions are exactly as in section III., and no constant is obtained. From (2), (3) and (4) another equation, similar to (12), could be developed in which K_4 enters but K_3 does not. But under these circumstances no assumption is made that C_h and C_e are in equilibrium; the conditions are the same as VIII. and no constant is obtained.

To state the problem of XI. in other words, can equations (8) and (12) hold simultaneously? To solve the question we must equate (8) and (12).

From (8) and (12), by identity and comparison,

$$\frac{K_1K_3V+K_2\sqrt{V}}{1+K_3}=\frac{K_3(K_1+K_1K_4)V}{K_4(1+K_3)}. \qquad (14)$$

From (14),

$$\frac{K_1}{K_2}=\frac{K_4}{K_3\sqrt{V}}$$

One of the 4 factors, K_1, K_2, K_3 and K_4, must be a function of the volume. They cannot all be constants. If they were constants we should have the anomalous case of a tautomeric substance giving an Ostwald constant, according to equation (8); a Rudolphi constant, according to equation (13); and no constant at all, according to equation (12). Such a state of affairs is manifestly impossible. It is certain, then, that we are not allowed to make all 4 assumptions involved in equations (1), (2), (3) and (4). We may make any three of them.

If the assumption in equation (1) is omitted, the case becomes like VIII. and no constant is obtained. If the assumption in equation (2) is not made the case becomes identical with III., and no constant is obtained. If the equation (3) is omitted, we obtain a Rudolphi constant according to equation (13). If equation (4) is left out, we obtain an Ostwald constant according to equation (8).

It has been proved, then, that it is impossible to have simultaneously, (*a*) equilibrium between the molecular forms of the tautomers, (*b*) equilibrium between the anions of the two tautomers, and (*c*) one tautomer obeying Ostwald's dilution law and the other obeying Rudolphi's equation.

The data obtained by measuring the conductivities of substances thought to be tautomeric can give us no decisive information whether the substance exists in only 1 tautomeric form or in 2 forms. The data do not tell us whether the 2 tautomeric forms change into each other quickly, or slowly, or at all. If a constant is obtained by substituting the proper figures in Ostwald's dilution formula we do not know from this fact alone whether there are 2 tautomeric forms or only 1; if there are 2, we do not know whether the equilibrium exists according to I., II., VI., IX., or XI(8). If a Rudolphi constant is found, this fact does not make it possible to decide

whether there is 1 tautomer or 2; if there are 2 tautomeric forms, we do not know whether the equilibrium is that of IV., V., VII., X. or XI(13). If no constant is obtained by substituting the proper data in either Ostwald's or Rudolphi's dilution formula, we still are in doubt as to whether there is 1 tautomer or 2; if we know from other facts that there are 2 tautomeric forms, we still do not know from the conductivity data whether the equilibrium is according to III. or VIII. We must learn in all cases whether there is a change in the equilibrium between the molecular, or ionic, forms with changes in dilution, changes in temperature, and changes in solvent. In order to study the problem of tautomerism more deeply, a combination of physical and chemical methods must be used. The physical methods will give light on some phases of the equilibrium and reaction phenomena, whereas chemical methods will, in many cases, give evidence on the other questions to be solved.

XII. All of the equations used above in considering the tautomeric acids can be used with tautomeric bases. To illustrate with a familiar example, the amidines are weak bases which react with strong acids and form salts. It is probable that both nitrogens have basic properties, the strength of the base corresponding to each depending upon the nature of the groups attached to that nitrogen.

$$\underset{\text{I.}}{RC{:}NR''(NHR')} \rightleftharpoons \underset{\text{II.}}{RC{:}NR'(NHR'')}$$

$$\underset{\text{III.}}{RC{:}N(HR')(OH)(NHR'')} \rightleftharpoons \underset{\text{IV.}}{RC{:}N(HR'')(OH)(NHR')}$$

Wheeler[1] has shown that probably no amidine has been isolated in 2 tautomeric forms, I. and II. Just as an amidine in solvents may then be considered to be a mixture of 2 forms, I. and II., in equilibrium, so the true bases corresponding to these amidines may be considered to be in molecular equilibrium as in Sections III. and IV. There are also other tautomeric possibilities besides III. and IV. which are not considered here.

[1] THIS JOURNAL, **19**, 367; **20**, 853; Ber. d. chem. Ges., **32**, 35. v. Pechmann: *Ibid.*, **28**, 869, 2362, etc. Walther: J. prakt. Chem., **58**, 41.

But especially must we recognize the substance having the formula $RC(NHR')(OH)(NHR'')$ as one of the possible forms in equilibrium with all of the other tautomeric forms; this substance, may, in fact, be an intermediate product in the change of III. into IV. The hydroxyl would then be considered as moving between the NHR′ group and the NHR″ group, just as the hydrogen of the molecular enol and keto forms of the urazoles moves from the nitrogen to the oxygen and back. Simultaneous with the shifting of the hydroxyl group there is a change in the position of the double bond between the carbon and a nitrogen. These bases III. and IV. could ionize according to the following equations:

$$\text{III. } RC{:}N(HR'OH)(NHR'') \underset{K}{\rightleftharpoons} \underset{\text{V.}}{RC{:}\overset{+}{N}(HR')(NHR'')} + \overset{-}{O}H$$

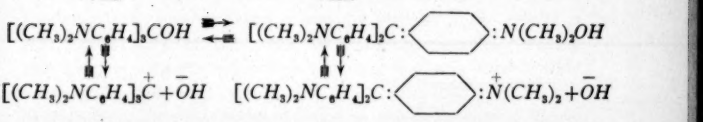
$$\text{IV. } RC{:}N(HR''OH)(NHR') \underset{K_1}{\rightleftharpoons} \underset{\text{VI.}}{RC{:}\overset{+}{N}(HR'')(NHR')} + \overset{-}{O}H$$

The values of K, K_1 and K_2 could vary very greatly, and it would take the equations in Sections I. to V. to express the quantitative tautomeric relations. If the cathions V. and VI. were in equilibrium, equations VI., VII. and VIII. would express the quantitative relations of the tautomers. The salts corresponding to these bases, III., IV., V. and VI., would be treated in the same way, but these salts would be more highly ionized.

Likewise the bases of the pararosaniline series almost certainly exist in 2 tautomeric forms. Hantzsch and Osswald[1] showed that the colored strong base, VIII., of hexamethylpararosaniline rearranges spontaneously into the colorless weak base, VII. But that there is an equilibrium between VII. and VIII. in solution can hardly be doubted, because the free base gives deeply colored salts, corresponding to VIII. and X., when it is treated with strong acids.

[1] Ber. d. chem. Ges., **33**, 278.

VII. VIII.

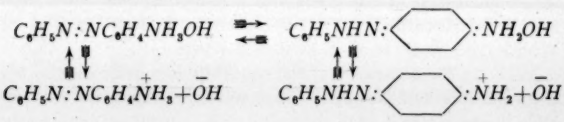


IX. X.

That the colored quinone base, VIII., is present in only a very small amount in equilibrium with a large amount of VII., is shown by the fact that solutions of pure hexamethyl-pararosaniline are practically colorless. But the carbinol, VII., gives only a minimum amount of cathions and hydroxyl ions (IX.), whereas the ammonium hydroxide derivative (VIII.) is a much stronger base. It is clear, then, that acids would act practically only on X. and not appreciably on IX., and colored salts of X. would be the chief product formed, together with a small amount of salt corresponding to IX. In the change then from the one tautomeric base, VIII., to the more stable one, VII., there is a shifting of the hydroxyl as in the amidines.

In the same way, such bases as amidoazobenzene and methyl orange[1] show themselves to be tautomeric bases.

XI. XII.



XIII. XIV.

The weak base, XI., exists in equilibrium with the strong base XII. Peculiarly enough, the vibration of a hydrogen atom apparently causes the change in basicity. As the amino-azobenzene is not deeply colored, it is probable that XII. is present to only a small extent in equilibrium with a large amount of XI., but since the quinone salts are salts of a fairly strong base, it is evident that the small amount of XII. present

[1] Julius Stieglitz: J. Am. Chem. Soc., **25**, 1119.

is highly ionized in comparison with XI. When a strong acid is added, then, to this solution a large amount of the colored quinone salt corresponding to XII. and XIV. is formed, together with a small amount of the less deeply colored azo salt XI and XIII.

All of the evidence at hand regarding these bases makes it appear probable that they exist in equilibrium conditions in solution, as illustrated above. Although, in the discussion above, it was assumed, for brevity, that the molecular forms are in equilibrium, the problem is as complicated with these tautomeric bases as it is with the tautomeric acids. But the writer would like to point out that the evidence is very inadequate and entirely insufficient to permit us to say with certainty that there is really equilibrium between a quinone and a colorless complex either in the free bases or their salts. Furthermore, there is not sufficient quantitative evidence on hand to enable us to see clearly the mechanism of the reactions involved in the changes from the colorless to the colored substances, or *vice versa*, or to say whether the changes are molecular or ionic, whether they take place directly or through intermediate stages. The ionic theory and the chromophoric theory have such a hold upon us that we attempt to interpret all of the above changes by means of them. They may contain a great deal of truth, but also a great deal that must ultimately be discarded. What we need is a large amount of quantitative work to help us find the truth.

XIII. In the discussion of the equilibrium conditions and affinity constants of the acids, bases and salts considered in I. to XII., it was assumed that the value of K_3 is attained practically instantaneously, whatever the initial conditions. But if during the measurement of the affinity constants by conductivity methods, a rearrangement of one tautomeric form into another is taking place slowly,[1] the value of the affinity constant will change with time when the affinity constants for the 2 tautomeric forms are different. If we consider the case under I., in which

[1] Wislicenus: Ann. Chem. (Liebig), **291**, 147; **312**, 34. Dimroth: *Ibid.*, **335**, 1; **338**, 143. Hantzsch and Schultze: Ber. d. Chem. Ges., **29**, 699, 2251. Busch and Oppenheimer: *Ibid.*, **37**, 2333.

$$\frac{H\times(C_{hi}+C_{ei})}{(C_h+C_e)}=\frac{(K_2+K_1K_3)V}{(1+K_3)}=KV,$$

we see at once that since K_3 does not enter alike into the numerator and denominator the value of K will change with change in value of K_3 and the determination of the velocity of the change of K will enable us to determine the velocity of the change of K_3. But if K_1 and K_2 are equal, the numerator and denominator will both contain the function $1 + K_3$, and K will be independent of the change of K_3 with time. Similar remarks apply to all of the other cases, and these will be discussed more fully in a subsequent article. All of the equilibrium conditions may change with change in solvent, temperature and other conditions.

XIV. The hydrolysis constant of a salt of a tautomeric, or other, acid or base which obeys Ostwald's dilution law is, according to Arrhenius,[1] Walker[2] and Shields,[3] $K_{hyd}=\frac{Kw}{Ka'}$, in which K_{hyd} is the hydrolysis constant of the salt, K_w the ion product of the water at the temperature used, and $K_{a'}$ the affinity constant of the acid, formed by hydrolysis, at the moment the hydrolysis is determined. It was shown above, in III., that the affinity constant, K_a, of a tautomeric acid, both of whose tautomeric forms give hydrogen ions according to Ostwald's dilution law, is derived from the following equation:

$$\frac{H\times(C_{hi}+C_{ei})}{(C_h+C_e)}=\frac{(K_2+K_1K_3)V}{(1+K_3)}=K_aV.$$

K_a is therefore equivalent to $\frac{K_2+K_1K_3}{1+K_3}$, in which it is recalled that K_1 is the affinity constant of the keto form, K_2 that of the enol form, and K_3 is the ratio of the amount of keto to enol form when K_a is determined.

The amount of hydrolysis, or the hydrolysis constant, of such a tautomeric salt depends upon a large number of factors.

[1] Z. physik. Chem., **5**, 1; **13**, 407.
[2] *Ibid.*, **4**, 319; **32**, 137. J. Chem. Soc., **77**, 5.
[3] *Ibid.*, **12**, 167.

A number of cases must be considered in detail. The question as to whether abnormal hydrolysis is possible depends, first, upon the rapidity with which the value of K_3 is established by the acid; secondly, upon the rapidity with which equilibrium is established between the 2 tautomeric forms of the salt, if the salt exists in 2 forms; thirdly, upon whether the value of K_3 is the same for salt and acid. All of the following reasoning applies equally as well to the salts of tautomeric bases.

The question as to the conditions affecting the hydrolysis of tautomeric compounds is one that has caused considerable discussion by Hantzsch,[1] Kauffmann[2] and Zawidzki.[3] Hantzsch and Barth determined the hydrolysis constants of a number of tautomeric salts and from these data calculated the affinity constants of the acids. But in nearly all cases the affinity constants determined from the hydrolysis measurements were much greater than those determined directly from the tautomeric acids by conductivity or other methods. Hantzsch and Barth therefore concluded that the salts of the acids have constitutions differing from those of the free tautomeric acids. In other words, they believed that the acid corresponding to the constitution of the salt differs from and is stronger than the original acid from which the salt was made. The original acid was therefore called a *pseudo* acid and the salt was said to have an abnormal hydrolysis constant. Kauffmann tried to show, by the application of the mass law, that Hantzsch and Barth's results and deductions are theoretically impossible, and not in harmony with the original assumptions and concluded that abnormal hydrolysis is yet to be explained. Zawidzki tried to show that Hantzsch is correct and that the ratio between the enol and keto forms in the acid can be determined from the data obtained by Hantzsch and Barth. As Kauffmann[4] has pointed out, however, Zawidzki made a mistake in his equations. Euler[5] has recently called Hantzsch's results into question.

[1] Ber. d. chem. Ges., **35**, 210; **39**, 2098.
[2] Z. physik. Chem., **47**, 618.
[3] Ber. d. chem. Ges., **37**, 2298.
[4] Ber. d. chem. Ges., **37**, 2468.
[5] *Ibid.*, **39**, 1607, 2265.

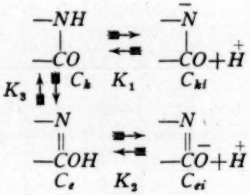
The above authors assumed that the constant of hydrolysis of a salt of a tautomeric acid which obeys Ostwald's dilution law is $K_{hyd}=\frac{K_w}{K_{a'}}$, in which K_{hyd} is the hydrolysis constant of the salt, K_w the ion product of water at the temperature used, and $K_{a'}$ the affinity constant of the acid, formed by hydrolysis, at the moment the hydrolysis is measured. They assumed that we have equilibrium between C_t and C_k, or that K_3 is constant when K_a is measured. The question of the abnormal hydrolysis of the salt depends upon the value of $K_{a'}$ for the acid liberated by hydrolysis, and this value of $K_{a'}$ depends upon the value of K_3 at the time the hydrolysis is determined. They assumed that if K_3 is the same in the acid liberated by hydrolysis as in the tautomeric acid whose affinity constant, K_a, is determined by conductivity or saponification methods there can be no abnormal hydrolysis. Let us now study this question of hydrolysis.

XV. One of the most important questions connected with tautomerism is that of the constitution of the salt or salts derived from a tautomeric acid or base. Are 2 tautomeric salts formed from the acid in solution, or only one? If 2, what is the ratio of the concentration of the anions of the 2 salts in comparison with the ratio of the concentrations of the anions in a solution of the acid alone? Does the ratio of the concentrations of the undissociated portions of the 2 salts differ from that for the acid, and does it change with change in time, in temperature, in solvent and change in the cathions, or change in salts? It may be stated again that much quantitative evidence is now at hand which proves that when 2 tautomeric forms of an acid in constant equilibrium are neutralized by a base there are generally 2 tautomeric salts formed in constant equilibrium.[1] The ratio of the undissociated keto and enol form varies with the salts, apparently somewhat with the solvents; although no variation with temperature or time generally occurs this may happen in some cases.[2]

What changes take place when a tautomeric acid is being

[1] Acree: THIS JOURNAL., **37**, 71.
[2] Wislicenus: Ann. Chem. (Liebig), **291**, 204, 211; **313**, 40.

neutralized with a base and all equilibrium conditions are established practically instantaneously? If we represent graphically the equilibrium for the acid and assume a case that



has been proved experimentally, namely, that

$$\frac{H \times C_{ki}}{C_k} = K_1 V, \tag{1}$$

$$\frac{H \times C_{ei}}{C_e} = K_2 V, \tag{2}$$

and

$$C_k = K_3 C_e; \text{ consequently, } C_{ki} = \frac{C_{ei} K_1 K_3}{K_2}. \tag{3}$$

It follows that

$$\frac{H \times (C_{ki} + C_{ei})}{(C_k + C_e)} = \frac{(K_2 + K_1 K_3)}{(1 + K_3)} = K_a V. \tag{4}$$

When a small portion of the base is added, the 2 tautomeric salts, that is the ions corresponding, are formed in the ratio of equation (3), $C_{ki} = \frac{C_{ei} K_1 K_3}{K_2}$.

Since the 2 tautomeric salts are dissociated to about the same extent, the ratio of the amount of molecular keto salt, formed from its ions, to that of the molecular enol salt is much less than K_3. There is a further physical-chemical reason, with many chemical examples, for thinking that the ratio K'_3 for the salt is less than K_3 for the acid. The sodium has the negative nitrogen of the

$$-\overset{-}{N}C{:}O \text{ or } -N{:}\overset{-}{C}O$$

group attracting it; but the more negative oxygen exerts a greater attraction, and hence, other factors not being considered, a greater portion of the undissociated salt has the enol form. It will be recalled that Hantzsch[1] showed that phenylnitromethane dissolves in alkalies and forms much

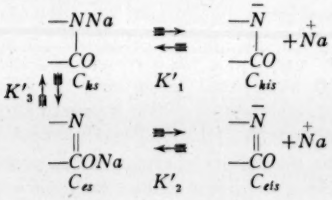
$$C_6H_5CH{:}N(O)ONa$$

and a small amount of

$$C_6H_5CHNaNO_2.$$

In general, the work of Hantzsch,[2] Wislicenus,[3] Dimroth[4] and of Acree[5] have shown that when a keto derivative is treated with an alkali the salt formed exists mostly as an enol form; K'_3 is, therefore, generally less than K_3.

The 2 salts formed have new equilibrium conditions peculiar to themselves, which must be represented as follows: C_{ks}, C_{es}, C_{kis}, and C_{eis} represent the number of gram molecules, or ion equivalents, of the keto salt, enol salt and their anions, respectively, in the volume V.



A new set of equations, similar to those for the acid, but having different values for the constants, express these rela-

[1] Ber. d. chem. Ges., **29**, 699, 2251. See also Hollemann: Rec. Trav. chim., **14**, 129. Acree: THIS JOURNAL, **37**, 71.

[2] Ber. d. chem. Ges., **32**, 634, 1723, 3066, 3089, 3101, 3132, 3137; **35**, 226, 1001; **38**, 1005; **39**, 1073, 1084, 2098.

[3] Ann. Chem. (Liebig), **291**, 147; **313**, 34. Ahren's Sammlung, **2**, 187.

[4] Ann Chem. (Liebig), **335**, 1; **338**, 143.

[5] THIS JOURNAL, **27**, 118; **31**, 185; **32**, 606; **37**, 71, 361. Ber. d. chem. Ges., **35**, 553; **36**, 2139; **37**, 184, 618.

tions. We shall here consider only one in which K'_3 is constant, which is usually true with the alkali salts of the tautomeric compounds studied up to this time. Let

$$\frac{N_a \times C_{kis}}{C_{ks}} = K'_1 V, \tag{5}$$

$$\frac{N_a \times C_{eis}}{C_{es}} = K'_2 V, \tag{6}$$

and

$$C_{ks} = K'_3 C_{es}; \text{ consequently, } C_{kis} = \frac{C_{eis} K'_1 K'_3}{K'_2}. \tag{7}$$

K'_3 may in some cases be equal to K_3, but will generally be much smaller. In alkali salts, K'_1 and K'_2 will have a value not far from unity, since alkali salts, even of weak acids, are highly ionized. $C_{ki}:C_{ei}$ changes in ratio, with increase of sodium hydroxide added from $\frac{K_1 K_3}{K_2}$ to $\frac{K'_1 K'_3}{K'_2}$.

Now let us examine the equilibrium conditions of the solution when exactly the equivalent amount of sodium hydroxide, or other base, has been added to the tautomeric acid. The solution now contains the 2 tautomeric salts whose relations are expressed by (5), (6) and (7). But since the tautomeric acids are weak, some hydrolysis of the salts is necessary and there is present a small amount of the 2 tautomeric acids, very little dissociated, which obey the requirements of (1), (2), (3), (5), (6), and (7). There is present also the equivalent amount of sodium hydroxide, nearly completely ionized.

What will be the affinity constant of the small amount of tautomeric acid under these conditions? According to (1), (2) and (3),

$$\frac{H \times C_{ki}}{C_k + C_e} = \frac{K_1 K''_3 V}{1 + K''_3}. \tag{8}$$

in which K''_3 is the ratio of the amount of the keto form to that of the enol form of the undissociated acid present with the salt.

The further discussion now depends upon the method of

obtaining the ratio between the 2 anions, C_{ki} and C_{ei}. We could attempt to get this ratio from (1), (2) and (3) and from (5), (6) and (7), whereby we should have

$$\frac{C_{ki}}{C_{ei}} = \frac{K_1 K_3}{K_2} = \frac{K'_1 K'_3}{K'_2}$$

which would give us relations concerning the values of the constants. This ratio

$$\frac{C_{ki}}{C_{ei}} = \frac{K_1 K_3}{K_2},$$

held for the solution of the acid alone, when all of the ions came from the acid. This followed from the 3 assumptions in (1), (2) and (3). But since the values in (1), (2) and (3) are now vanishing, it seems that we should consider the ions as coming practically wholly from the 2 tautomeric salts. But new relations hold for the ratio of the ions from the salts. It follows from (5), (6) and (7) that

$$\frac{C_{ki}}{C_{ei}} = \frac{K'_1 K'_3}{K'_2}, \qquad (9)$$

and from (8) and (9), by substitution, that

$$\frac{H \times C_{ei}}{C_k + C_e} = \frac{K'_2 K_1 K''_3 V}{K'_1 K'_3 (1 + K''_3)}. \qquad (10)$$

From (8) and (10), by addition, it follows that

$$\frac{H \times (C_{ki} + C_{ei})}{(C_k + C_e)} = \frac{K_1 K''_3 (K'_1 K'_3 + K'_2) V}{K'_1 K'_3 (1 + K''_3)} = K_{a'} V. \quad (11)$$

But from (1), (2) and (3), for the free acid,

$$\frac{H \times (C_{ki} + C_{ei})}{(C_k + C_e)} = \frac{(K_2 + K_1 K_3) V}{1 + K_3} = K_a V. \qquad (12)$$

The affinity constant of the acid formed by hydrolysis of a tautomeric salt may be greater than, equal to, or less than that of the free acid.

But $K_{hyd} = \frac{K_w}{K_{a'}}$, in which K_{hyd} is the hydrolysis constant for the salt, K_w the ion product for water at the temperature and $K_{a'}$ the affinity constant of the acid present in the solu-

tion. If we now examine K_a in (12), and we remember that in most tautomeric compounds studied up to this time K_3 is large, while K_1 and K_2 are small, we see that K_a is small. But $K_{a'}$ in (11) becomes practically

$$\frac{K_1(K'_2+K_1'K_3')}{K_1'K_3'}$$

when K''_3 is large and practically equal to K''_3+1. Since the denominator involves K'_1, the affinity constant for a salt which is around unity, and K'_3, which all experimental evidence leads us to believe to be generally much smaller than K_3, we see that $K_{a'}$ is probably generally larger than K_a. When $K_{a'}$ is larger than K_a the hydrolysis constant, $K_{hyd}=\frac{K_w}{K_{a'}}$, is smaller than $\frac{K_w}{K_a}$ calculated for the free acid with the affinity constant K_a. This then accounts for the abnormal hydrolysis reported by Hantzsch,[1] and for which no explanation was forthcoming up to this time. When, however, the value of $K_{a'}$ is near that of K_a the experimental methods used by Shields,[2] Walker[3] and Koelichen,[4] are not sufficiently accurate to enable us to determine that the value of $K_{a'}$ is essentially different from that of K_a. In other words, the tautomeric salt will show practically a normal hydrolysis.

When $K_{a'}$ becomes very much smaller than K_a, K_{hyd} becomes larger than that calculated from $\frac{K_w}{K_a}$ and the salt shows an abnormally large hydrolysis.

The following example will illustrate the conditions under which the hydrolysis of a salt of a tautomeric acid may be abnormally low. Suppose that K_3 for the acid (see Section I.) is 100, while K_2 is equal to 100 K_1. Then from I., 6,

$$\frac{C_{hi}}{C_{el}}=\frac{100K_1}{100K_1}=1.$$

[1] Ber. d. chem. Ges., **35**, 210.
[2] Z. physik. Chem., **12**, 167.
[3] *Ibid.*, **4**, 319; **32**, 137. J. Chem. Soc., **77**, 5.
[4] Z. physik. Chem., **33**, 129.

If in the tautomeric salts K'_3 is $^1/_{10}$, since K'_1 and K'_2 for such salts are nearly alike and around the value 1, $\frac{C_{kis}}{C_{eis}} = {}^1/_{10}$ for the salts. K_a for the acid is then

$$\frac{K_2+K_1K_3}{1+K_3} = \frac{200K_1}{101} = 2K_1.$$

$K_{a'}$ for the acids formed by hydrolysis of the salts, since practically all of the ions come from the salts, is (XV., 11) $11K_1$, or about 5 times as large as K_a. It is, therefore, evident that the hydrolysis constant, $\frac{K_w}{K_{a'}}$, for the tautomeric salt is one-fifth as large as that calculated from $\frac{K_w}{K_a}$ for the acid.

We can also calculate the value of K''_3 for the acid in the presence of the salt. K_3 is at first 100. If we take $V = 1$, and call H the concentration of the hydrogen ions,

$$C_e = \frac{H \times C_{ei}}{100K_1}, \qquad (13)$$

and

$$C_k = \frac{H \times C_{ki}}{K_1}. \qquad (14)$$

But $C_{ei} = 10C_{ki}$. Then from (13),

$$C_e = \frac{H \times 10C_{ki}}{100K_1} = \frac{H \times C_{ki}}{10K_1}. \qquad (15)$$

Then from (14) and (15), by division, $\frac{C_k}{C_e} = 10$ instead of 100. In other words, the change of a tautomeric acid, the 2 forms of which give hydrogen ions, into the tautomeric salts causes a change in the value of K_3 for the acid present with the salt, provided K'_3 is different from K_3.

XVI. Suppose, however, that only 1 tautomeric salt is formed from a tautomeric acid, only 1 tautomeric form of which gives hydrogen ions. Assuming that all equilibrium changes in the salt and acid take place practically instanta-

neously, will the hydrolysis of this salt in aqueous solution be normal or abnormal? This one case has already been considered by Hantzsch, Kauffmann, Euler and Zawidzki. Hantzsch decided that the hydrolysis can be abnormal, but Kauffmann showed by the application of the mass law that the hydrolysis should be perfectly normal. Suppose that the sodium salt in the solid state has the enol form. When it is dissolved in water, it is at once partly hydrolyzed into sodium hydroxide, nearly completely ionized, and the enol tautomeric acid. The extent of the hydrolysis at this stage is dependent simply upon the value of the affinity constant K_2 for the enol acid, and is obtained from $K_{hyd}=\frac{K_w}{K_2}$. But the enol acid liberated immediately begins to rearrange into the keto form. If the keto form is not an acid, hydrogen ions disappear and the hydrolysis of the sodium salt becomes greater until the equilibrium is finally established. The hydrogen and hydroxyl ions come from the water. These changes, by assumption, take place too quickly to be experimentally measured. But if the rearrangement of the enol acid, librated by hydrolysis of the salt, were to take place very slowly the hydrolysis of the salt would at first be measurably abnormally small, and would approach its normal value hand in hand with the change of the enol acid into the keto form. As Kauffmann has already applied the mass law to the solution of this problem, this will not be done here.

XVII. Suppose that the free tautomeric acid exists in solution in 2 tautomeric forms, which give ions, and suppose that K_1 for the keto acid is small in comparison with K_2 for the enol acid. Suppose that the salt can be isolated in the solid state as only enol salt which does not rearrange *per se* to keto salt or does so only very slowly. The moment the salt is dissolved in water, the acid liberated by hydrolysis is enol acid with the affinity constant K_2, and the hydrolysis constant of the salt is small and can be calculated from K_2. But immediately after the enol acid is liberated it rearranges partly into the keto acid with the affinity constant K_1, and hydrogen ions disappear. The hydrogen ions formed by the ionization of this

keto acid are then neutralized by the hydroxyl ions present and some keto salt and its ions are formed. These processes then continue until the enol salt is changed to some extent, into keto salt, and the tautomeric acid existing as hydrolysis product, practically undissociated, has reached the equilibrium condition, and the ion product for water is established. In this case, then, there will be an increase in the hydrolysis constant from $\frac{K_w}{K_2}$ to $\frac{K_w}{K_{a'}}$, in which $K_{a'}$ represents the affinity constant of the acid present when equilibrium is finally established. When these changes take place within a few seconds the change in hydrolysis will be too rapid to admit of measurement, but when the changes take place slowly the reaction can be studied quantitatively.

If the salt is isolated as the keto salt, and is dissolved in water, the acid liberated by hydrolysis is the keto acid with the affinity constant K_1. The hydrolysis constant for this salt is much larger than that for the enol salt and also larger than that for the tautomeric salts when equilibrium is established. The keto acid liberated at once rearranges partly into enol acid. The hydrogen ions from this are neutralized by the hydroxyl ions present and some enol salt is formed. These processes continue, as discussed in the preceding case, till the same equilibrium is established as is formed in the preceding case, and the hydrolysis constant is lowered from the value $\frac{K_w}{K_1}$ to $\frac{K_w}{K_{a'}}$. When the keto salt is first dissolved, it shows an abnormally high hydrolysis constant, which, according to the hypothesis, is lowered to the normal value for the tautomeric acid too quickly to permit of measurement. If the processes were to take place slowly, however, the change in hydrolysis constant could be easily measured.

The change of the enol salt into the keto form, and *vice versa*, may take place not only through intermediate hydrolysis and rearrangement of the liberated acid, as discussed above, but may do so directly by the change of one undissociated form of the salt into the other. Acree[1] has shown that in cer-

[1] This Journal, **37**, 71.

tain urazole salts the undissociated portion of the keto salt is in equilibrium with the non-ionized enol form. The anions are not in equilibrium. The 2 urazole salts change into each other practically instantaneously. In other cases it may be found that the change is very slow[1] under certain conditions of solvent and temperature, and in still other cases it may be found that the anions are in equilibrium.

If the tautomeric salts were obtained as a mixture of keto and enol salts in a ratio necessary to give equilibrium for the salt when it is dissolved, then no change in hydrolysis would take place with time after the solution is made. The salt would at once give the normal hydrolysis constant peculiar to itself.

But if the ratio of the 2 forms of the salt in the solid state is different from that which they must have to give equilibrium at once, there will be a change in the hydrolysis of the salt after it is dissolved, and a simultaneous change in the ratio of the 2 salts. This is well illustrated by the example of the α- and β-copper salts of ethyl formylphenylacetate, both of which can be isolated and changed into each other slowly.

XVIII. There will be abnormal hydrolysis when a molecular quantity of sodium hydroxide is added to a solution of a tautomeric acid, the 2 forms of which have different affinity constants and change very slowly into each other under the conditions of the experiment, provided that the 2 tautomeric forms of the acid are not already present in the ratio necessary for the equilibrium of the system. This is well illustrated by 2 examples worked out by Dimroth and Hantzsch and Pilat.

Dimroth[2] found that when the keto form of methyl phenyl-1,2,3-triazole-5-oxy-4-carboxylate in water is treated with a molecular quantity of sodium hydroxide the alkali is neutralized only very slowly as the weak keto acid changes into the strong enol acid. At first there is abnormally high hydrolysis which gradually becomes normal. But if some organic solvent is added in which the keto form rearranges much more rapidly, the abnormal hydrolysis becomes normal so quickly that the velocity can hardly be measured.

[1] Wislicenus: Ann. Chem. (Liebig), **291**, 204, 211; **313**, 40.
[2] Ann. Chem. (Liebig), **335**, 1; **338**, 143.

Hantzsch and Pilat[1] found that a solution of secondary sodium cyanurate and a molecular quantity of sodium hydroxide contains much free alkali. But if the solution is heated, tertiary sodium cyanurate is formed on account of the rearrangement of the weak keto acid into the strong enol form at the higher temperature.

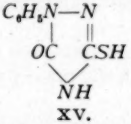
Hantzsch and Shultze[2] found that phenylnitromethane dissolves very slowly in carbonates, the reaction depending upon the rearrangement of the neutral phenylnitromethane into the acid iso form.

These experiments illustrate, in the clearest way, that in determining whether a salt shows abnormal hydrolysis it must certainly be known (1) that equilibrium has been established in the solution of the tautomeric salt or salts when the hydrolysis is measured, (2) that equilibrium has been established in the solution of the tautomeric acid when its affinity constant is measured, and (3) that all the conditions of temperature, solvent, etc., are the same in (1) and (2). If the conditions in (1), (2) and (3) are not observed, an apparent abnormal hydrolysis might easily be found.

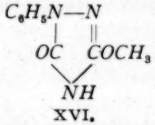
Phenylurazole and 1-phenyl-3-thiourazole are moderately strong acids. Both color litmus red, and with ferric chloride they give colored salts. Mr. Shadinger has proved that the 2,3(enol)-amide group of phenylurazole has an affinity constant $K = 0.00001$, whereas the 4,5(keto)-amide group has a constant $K = 0.00000005$; in other words, the 2,3-amide group has an affinity constant 200 times as large as that of the 4,5-amide group. It was, of course, to be expected that the enol group would be a much stronger acid than the 4,5-keto-amido group, and this confirmation of the former results obtained by purely chemical means, by those now obtained by physico-organic methods is very satisfactory. The 2,3-amide group is the one first attacked when phenylurazole is alkylated or acylated, and, in general, seems to be more reactive than the 4,5-amide group. Although both of these urazoles have 2 hydrogen atoms that, under the proper conditions, can be re-

[1] Ber. d. chem. Ges., **38**, 1005. Dissertation, Leipzig, 1905.
[2] Ber. d. chem. Ges., **39**, 699, 2251.

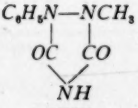
placed by metals, or by alkyl or acyl groups, yet these urazoles titrate nearly quantitatively as monobasic acids when treated with standard alkali in the presence of phenolphthalein. Even when we use Poirier's Blue, which is extremely sensitive to hydrogen ions, no evidence of a second hydrogen ion in these 2 urazoles is obtained. When, however, the first hydrogen ion of phenylurazole or 1-phenyl-3-thiourazole is replaced by an alkyl group, the resulting urazole shows decidedly acid properties. When 1-phenyl-3-methoxyurazole,



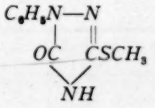
XV.



XVI.



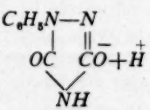
XVII.



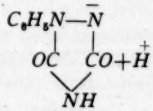
XVIII.

XVI., 1-phenyl-2-methylurazole, XVII., or 1-phenyl-3-thiomethylurazole, XVIII., is treated with 0.1 N alkali in the presence of phenolphthalein, approximately 0.95 molecular quantity of alkali can be added before the red color appears.

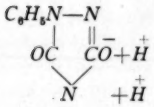
It is clear, then, that these urazoles ionize in steps, just as many other dibasic acids do. When phenylurazole is dissolved in water it ionizes chiefly according to XIX. and very little according to XX., XXI., XXII., etc., as will be discussed later.



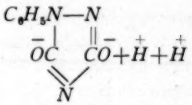
XIX.



XX.

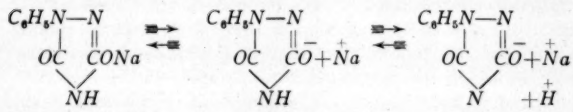


XXI.



XXII.

So when phenylurazole is titrated with 1 molecule of alkali the salt XXIII. is formed nearly to the exclusion of the other possible tautomeric salts. As has been pointed out by Noyes[1]



XXIII. XXIV. XXV.

and by Ostwald,[2] the salt XXIII. should be a very much weaker acid than the similarly constituted methyl derivative XVI. As a result, the methyl derivative titrates against 0.95 molecule alkali before it shares the alkali perceptibly with the phenolphthalein. The sodium salt, XXIII., is a very weak acid and gives very few hydrogen ions according to XXV., and it shares the alkali so largely with the phenolphthalein that 1 drop excess of 0.1 N alkali colors a solution of the sodium salt, XXIV., and phenolphthalein red.

Solutions of the alkali salts of phenylurazole, or of any of its alkyl derivatives, or of any 1-phenyl-3-thioalkylurazoles, XVIII., color methyl orange brown, and the metal in these solutions can be estimated practically quantitatively by titration with standard hydrochloric acid. Phenyl-3-thiourazole colors methyl orange red and the salts cannot be analyzed by the above method.

In fact, we can calculate approximately the amount of suppression of ionization exerted upon the 4,5-amide group of phenylurazole by the 2,3-amide group or its sodium salt. We

[1] Z. physik. Chem., **11**, 495; **13**, 417. Trevor: *Ibid.*, **10**, 321.
[2] *Ibid.*, **3**, 369.

have proved, from theoretical grounds and by experiment, that weak tautomeric acids, such as the 4,5-amide group, obey Ostwald's dilution law and that equation (1) expresses the equilibrium between the molecular (keto and enol) forms of the 4,5-amide group and their ions.

$$\frac{H \times U_i}{U_m \times V} = K. \qquad (1)$$

H represents the number of gram equivalents of the hydrogen ions, U_i the number of gram equivalents of the (keto and enol) urazole ions, U_m the number of gram molecules of the (keto and enol) urazole molecules, V the volume, and K a constant. It follows then that in a solution of phenylurazole, in which the 2,3-amide group suppresses the ionization of the 4,5-amide group, the condition of equilibrium of the 4,5-group is to be expressed by the equation (2).

$$\frac{(H'-y)(U_i-y)}{(U_m+y)V} = K, \qquad (2)$$

in which H' now represents the total number of gram equivalents of the hydrogen ions from both the 2,3- and the 4,5-amide groups, y the number of gram equivalents of the 4,5-urazole ions and its equivalent of hydrogen ions which have been changed to the molecular form in the suppression of the ionization of the 4,5-amide group. From the experimental data worked out by Mr. Shadinger it is possible to solve the above equations. When V equals 1024 liters the 2,3-amide group of phenylurazole is almost exactly 10 per cent dissociated, and the 4,5-amide group, when not influenced by the 2,3-amide group, is 0.7 per cent dissociated, or gives 1/14 as much hydrogen ions per gram molecule. In equation (1) the values of H and U_i are the same. The value of H' in equation (2) is evidently $15H$, U_i is the same as in (1) or is (H), U_m is $(1-H)$ in both (1) and (2) and equation (2) assumes the form (3),

$$\frac{(15H-y)(H-y)}{(1-H+y)} = KV. \qquad (3)$$

Since the denominator is practically unity, it follows that the

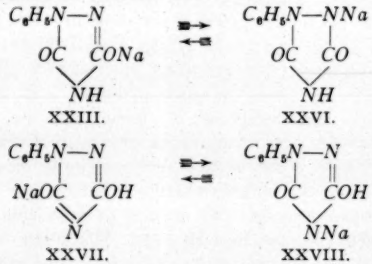
value of $H—y$ must become approximately $H/15$. In other words, the ionization of the 4,5-amide group is suppressed by the 2,3-amide group to 1/15 its normal amount. Since normally the 4,5-amide group gives only 1/14 as much hydrogen ions as the 2,3-amide group, it is evident that in a 0.001 N solution of phenylurazole the 2,3-amide group gives approximately 210 times as much hydrogen ions as the 4,5-amide group. This discussion, of course, does not take into consideration the slight suppression of the ionization of the 2,3-amide group by the weakly acid 4,5-amide group. That practically all of the hydrogen ions come from the 2,3-amide groups of phenylurazole and phenyl-3-thiourazole is made further evident by the fact that Mr. Shadinger has shown that 1-phenyl-4-methylurazole has practically the same affinity constant as phenylurazole, and 1-phenyl-4-methyl-3-thiourazole is as strong an acid as phenyl-3-thiourazole. When a solution of phenylurazole is titrated with a molecular quantity of alkali, approximately 99.5 per cent of the alkali is used up in neutralizing the 2,3-amide group and 0.5 per cent in neutralizing the 4,5-amide group. We are, therefore, justified, for purposes of ordinary discussion, in speaking of the monoalkali salts as having the constitution XXIII.

It follows, then, that the 4,5-amide group in sodium phenylurazole must be a very much weaker acid than the corresponding group in phenylurazole. Trevor,[1] Noyes[2] and Smith[3] have shown that the acid salts of dibasic acids give only a minimal amount of hydrogen ions. When a small volume of alkali solution is added to a solution of the sodium phenylurazole and phenolphthalein the alkali is shared between the weak acids, sodium phenylurazole and phenolphthalein, and the solution turns pink in color. The per cent of hydrolysis of the disodium phenylurazole, and other urazole salts, will be investigated.

But salt XXIII. is not the only one formed when a solution of phenylurazole is titrated with alkali. When only one molecular quantity of alkali is used the 4 salts, XXIII., XXVI.,

[1] Z. physik. Chem., **10**, 321.
[2] *Ibid.*, **11**, 495; **13**, 417.
[3] *Ibid.*, **25**, 144, 193.

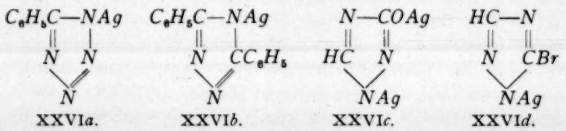
XXVII. and XXVIII., and their ions, are formed, XXIII. being the one present in greatest quantity.



XXIII. XXVI.

XXVII. XXVIII.

Since the keto form, —NHCO—, IV., of the 2,3-amide group of phenylurazole is in equilibrium with the enol form, —N:C(OH)—, II., it follows that each one of these forms will titrate against alkali. That the nitrogen (keto) salts, XXVI., will be formed is certain from the fact that the corresponding very stable tetrazole and triazole salts, XXVI*a*., XXVI*b*., XXVI*c*., XXVI*d*., and others, can be made very easily.[1] The amount



XXVI*a*. XXVI*b*. XXVI*c*. XXVI*d*.

of each salt formed at the beginning of the titration depends upon the ratio of the keto to the enol form and upon the strength of each as an acid. The same can be said of the 4,5-amide group and it follows that the relative amounts of XXIII., XXVI., XXVII. and XXVIII. formed will depend (1) upon the amount of each acid present of which these salts are derivatives, (2) upon the strengths of these acids, and upon the relative sup-

[1] Lossen: Ann. Chem. (Liebig), **263**, 105. Lossen and Statius: *Ibid.*, **298**, 92. Pinner: *Ibid.*, **297**, 248. Manchot and Noll: *Ibid.*, **303**, 33; **343**, 1. Manchot: Ber. d. chem. Ges., **31**, 2444. Widman and Cleve: *Ibid.*, **31**, 379. For benzamidine silver salt, see Pinner's Imidoether, 1892, p. 155.

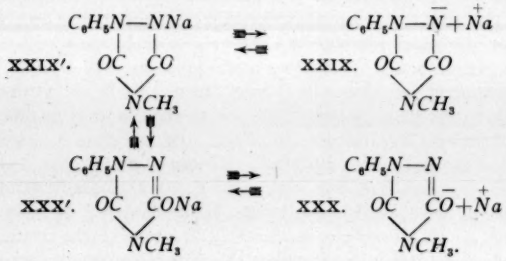
pression of the ionization of each acid by its corresponding salt and upon other conditions discussed in Sections XXIII. to XXVII., inclusive. There will be present also small amounts of the corresponding disodium salts and the non-ionized acids. The above formulæ do not take into consideration the tautomeric relationships of the amide groups not containing the metal. It has further been proved[1] that the molecular enol forms of salts XXIII. and XXVII. are in equilibrium with the molecular keto forms of the salts, XXVI. and XXVIII., respectively. It has been found that the salts of the 2,3-amide group and the salts of the 4,5-amide group are alkylated with about the same readiness. It therefore follows that when we treat sodium phenylurazole with alkyl halides, alkyl sulphates and acyl chlorides, since the 2,3-amide group contains nearly all of the sodium, we should get chiefly derivatives of the 2,3-amide group. This has been amply verified by the experimental evidence. When sodium phenylurazole[2] is heated in alcoholic-water solution with alkyl halides or alkyl sulphates, much 1-phenyl-2-alkylurazole, XVII., and a smaller amount of 1-phenyl-3-alkoxyurazole, XVI., are formed. The silver salt of phenylurazole gives a higher percentage of the 1-phenyl-3-alkoxyurazole, XVI., than does the sodium salt, and other salts give other ratios of the *N*-ester and the *O*-ester. Likewise, when the silver salt of phenylurazole is treated with acetyl chloride the chief product is 1-phenyl-2-acetylurazole.[3]

The writer made 1-phenyl-2-methylurazole and 1-phenyl-2-acetylurazole in this way. Since then Dr. R. F. Brunel and the writer have prepared, by this method, a large number of 1-phenyl-2-alkylurazoles, in which the alkyls are ethyl, propyl, isopropyl, butyl, isobutyl and isoamyl groups.

As has been published in a previous paper, the experimental evidence at hand, worked out by Mr. R. F. Brunel, J. M. Johnson and G. H. Shadinger, under the direction of the writer, all tends to establish the fact that the salts of tautomeric compounds exist in 2 forms,[4] whose molecules, XXIII. and XXVI.,

[1] Acree: THIS JOURNAL, **37**, 71.
[2] Acree: *Ibid.*, **37**, 79.
[3] Acree: *Ibid.*, **31**, 188; **32**, 609. Ber. d. chem. Ges., **36**, 3143.
[4] Acree: THIS JOURNAL, **37**, 78.

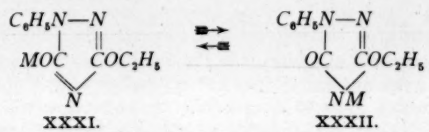
are in equilibrium and whose ions react with alkyl halides to give the corresponding *O*-esters and *N*-esters. It has been proved that in the alkylation of the salts of 1-phenyl-4-methylurazole neither the *O*-ester nor the *N*-ester is formed from the other according to Wheeler's[1] rearrangement theory. The *O*-ester is formed from the ion XXX directly, and the *N*-ester directly from the ion XXIX. The *N*-ester is not formed indirectly through an intermediate addition-product, as has been supposed by Nef[2] and by Michael.[3] The evidence leads us to believe that both the *O*-ester and the *N*-ester are formed by independent side reactions from the ions of the salts corresponding to XXIX and XXX. The quantitative data obtained with the urazoles point clearly to the fact that during these alkylations equilibrium is established practically instantaneously between the molecular forms of the salts, XXIX′ and XXX′. The fact must not be lost sight of, however, that it may be found later that the salts of other tautomeric compounds may establish their equilibrium only very slowly.[4] In some other cases this reaction may be complicated by the rearrangement of one ester into the other,[5] or into some other product. The reactions by which the esters are formed from the salts and the alkyl halides are those of the second order.



[1] Wheeler and students: *This Journal.*, **21**, 187; **23**, 135; **30**, 28.
[2] Ann. Chem. (Liebig), **266**, 52; **276**, 200; **277**, 59, 83, etc.
[3] J. prakt. Chem., **37**, 469; **45**, 580; **46**, 189, etc.
[4] Wislicenus: Ann. Chem. (Liebig), **291**, 204, 211; **313**, 40.
[5] Wheeler and students: This Journal, **21**, 185; **23**, 135; **30**, 28.

It is of interest to note that when the mono-metallic salts XXIII., is treated with an alkyl halide, some phenyldialkylurazole[1] and phenylurazole are formed. When silver phenylurazole is treated with ethyl iodide in ether solution considerable 1-phenyl-3,5-diethoxyurazole and phenylurazole are formed along with other products, which are now under investigation. This would, at first sight, appear to be a peculiar reaction. But the reason becomes at once clear if we remember that the phenylalkylurazole first formed, XVI. or XVII., is also an acid and takes part of the silver away from silver phenylurazole, giving phenylurazole and (for example) silver phenyl-3-ethoxyurazole. Toward the end of the reaction this side reaction becomes considerable and the silver phenyl-3-ethoxyurazole constantly reacts with the ethyl iodide and forms 1-phenyl-3,5-diethoxyurazole. That this is the correct interpretation of the reactions by which the phenyldialkylurazoles are formed was proved conclusively by establishing experimentally (1) that silver phenylurazole and ethyl iodide give phenyl-3-ethoxyurazole, (2) that silver phenylurazole and 1-phenyl-3-ethoxyurazole react and form phenylurazole and silver phenyl-3-ethoxyurazole, and (3) that silver phenyl-3-ethoxyurazole and ethyl iodide react readily and form 1-phenyl-3,5-diethoxyurazole.[2]

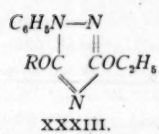
It has been found likewise that the salts of 1-phenyl-3-ethoxyurazole, XXXI. and XXXII., react readily with alkyl halides and alkyl sulphates and form both *N*-esters, XXXIV., and *O*-esters, XXXIII.



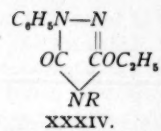
XXXI. XXXII.

[1] Acree: Ber. d. chem. Ges., **36**, 3148. Wheeler and Johnson: THIS JOURNAL, **30**, 24.

[2] Acree: Ber. d. chem. Ges., **38**, 3148.



XXXIII.



XXXIV.

The silver salt gives with ethyl iodide, in ether solution, almost exclusively 1-phenyl-3,5-diethoxyurazole, but the potassium salt with methyl iodide, in water-alcohol solution, or with dimethyl sulphate in water solution, gives almost entirely 1-phenyl-3-ethoxy-4-methylurazole, together with a small amount of the 1-phenyl-3-ethoxy-5-methoxyurazole. When the 1-phenyl-3-ethoxy-4-methylurazole is evaporated with alcoholic hydrochloric acid the ethoxy group is saponified and 1-phenyl-4-methylurazole is formed. By the above series of reactions we should be able to prepare other 1-phenyl-4-alkylurazoles from 1-phenyl-3-ethoxyurazoles. Mr. R. F. Brunel has confirmed this by experiment and will report later in detail.

A general discussion of the formation, rearrangement and reactions of the acetyl derivatives of the urazoles will be found in the experimental portion.

EXPERIMENTAL PART.

Carbethoxyphenylsemicarbazide, $C_6H_5N(COOC_2H_5)NHCONH_2$.—This substance[1] was prepared by the action of ethyl chlorcarbonate on phenylsemicarbazide in acetic ether solution. As has already been recorded, the compound occurs in 2 modifications, which melt at 172° and at 154°, and which can be changed into each other. When the substance precipitates out immediately from the acetic ether solution in which it is prepared it melts at 172°. But if, for some reason, it does not crystallize out at once, and if the solution must be evaporated, the substance will probably melt at 154°. When either of these 2 forms is crystallized from hot water the substance obtained melts at 154°. It was not known at first whether these modifications are enol

[1] This Journal, **27**, 127. Ber. d. chem. Ges., **35**, 556; **36**, 3145; **37**, 621. Rupe: Ber. d. chem. Ges., **32**, 12; **36**, 1104. Wheeler: This Journal, **27**, 270.

and keto, or other chemical forms, or simply physical isomers. Both forms, however, react practically alike toward ferric chloride, alkalies, and acetyl chloride, and show the same molecular weight in aqueous solution. Furthermore, either of them can be changed into the other by crystallization from the proper solvent. The 2 modifications have different solubilities in water. All these facts make it appear probable that these 2 forms are merely physical modifications and in no important way chemically different.

The determination of the molecular weights of these 2 forms in water solution was made by means of McCoy's apparatus. The formula used for calculating the molecular weights is that used by McCoy,[1] *viz.*, $M=\frac{WT}{\Delta V}$. W is the weight of the substance, Δ the elevation of the boiling point, and V the volume of the solution. T is a constant having a different value for each solvent; the value for water is 540.

In order to determine whether either form has the single molecular weight, the first readings were made very quickly.

Molecular Weight of the 154° M. P. Modification.

0.7820 gram substance, m. p. 154°, was used.

Rise in boiling point.	Volume of solution at boiling point, about 95°.	Molecular weight found.
0.86	22.5	218
0.83	22.7	224
0.83	24.0	212
0.80	24.0	220
0.78	24.5	221
0.80	24.8	213
	Average,	218
	Mol. wt. calculated,	224

On cooling, the solution deposited crystals which melted at 153°–155°.

[1] THIS JOURNAL, **23**, 358.

Molecular Weight of the 172° M. P. Modification.

0.4830 gram substance, m. p. 172°, was used.

Rise in boiling point.	Volume of solution at boiling point, about 95°.	Molecular weight found.
0.62	22.4	236
0.67	22.6	217
0.66	23.2	215
0.65	23.4	216
	Average,	221
	Mol. wt. calculated,	224

On cooling, the solution deposited crystals which melted at 153°–155°.

Both of the modifications seem to have practically the same molecular weight in aqueous solution, namely, that of the monomolecular form of the substance. If either of the modifications has a double molecular form in the solid state, it changes too quickly to the monomolecular form, when dissolved in water, to allow us to secure evidence on this point by the above method.

When heated in the solid state the higher melting isomer is the stable one; the lower melting form is changed into the higher melting form very rapidly at about 155°. When a small amount of the isomer which melts at 172° is mixed with a large amount of the form which melts at 154°, the melting point of the mixture is 172°. When the compound which melts at 154° is melted completely, or is only partially melted and is allowed to solidify at or below 153°, it then melts at 172°.

The change of one of these modifications into the other by crystallization from solvents seems to depend upon conditions of temperature, time and the solvent used, as the following experiments show: The writer is indebted to Mr. W. R. Travers, of the University of Utah, for aid in many of these experiments. When 1 gram of the form which melts at 172° was boiled in water 2 hours, or even 12 hours, it crystallized out in a granular state and melted at 153°–155°. Crystallization of the form which melts at 154° from hot

water did not change its melting point. The form which melts at 154°, then, is the one always obtained when the substance is crystallized from hot water. When solutions of the 2 forms were made by shaking them 48 hours with cold water, and the undissolved solids were filtered out, the melting points of these portions were still 172° and 154°. When the filtrates were evaporated *in vacuo* over sulphuric acid, they both yielded the isomer which melts at 154°. When these solutions were evaporated at 95° and the residues were dried at 110°, they then melted at 172°, probably because at 110° they were at least partly converted into the higher melting isomer. Mere contact with water does not change the melting points of the solids.

When the form which melts at 172° was crystallized from acetic ether it melted at 171°–172°. When the form which melts at 154° was crystallized quickly from acetic ether it melted at 153°–155°; but if boiled 3 hours in acetic ether and crystallized out at once, it melted at 171°–172°; but if this same solution were allowed to evaporate spontaneously for 48 hours, the precipitate melted at 154°–156°. It will be recalled that similar phenomena were observed in the preparation of carbethoxyphenylsemicarbazide. The higher melting form, then, seems to be the more stable one when the substance was crystallized from hot acetic ether.

When the form which melts at 172° was crystallized from acetone it melted at 154°. When crystallized from a mixture of alcohol and acetic ether it melted at 153°–156°. When crystallized from benzene it melted at 172°.

As the form which melts at 154° is the one always obtained when the substance is crystallized from water, it was thought that possibly this form is less soluble in water than the form which melts at 172°. At the writer's suggeston, Mr. W. R. Travers made some determinations of the solubilities of these 2 modifications in water. Pure powdered samples of the 2 forms were shaken with water for 48 hours in a thermostat at 20°, and the solutions were then filtered. The residues still melted at 172° and 153°–155°. Weighed quantities, about 30 grams, of each filtrate were evaporated in platinum

dishes at 95° and dried at 110°. The residues were slightly brown: the one from the form which originally melted at 172° still melted at 172° and the one from the isomer melting at 154° melted at 168°. The data showed that 1 gram of solution from the form which melts at 172° contained 0.0019 gram substance, whereas 1 gram of solution from the isomer which melts at 154° contained only 0.00146 gram substance. The lower melting form, then, is the less soluble one. In order to determine if there were any difference in the amounts of substance in the solutions of the 2 forms that had been boiled, Mr. Travers examined the solutions used in making the molecular weight determinations reported above. These solutions were allowed to stand at 15°.5 for 72 hours. Both solutions deposited crystals melting at 154°. One gram of the solution made from the substance melting at 172° contained 0.0012 gram substance; 1 gram of the solution made from the substance melting at 154° contained 0.0013 gram. Practically the same amounts, then, are contained in these 2 solutions; furthermore, these solubilities for the substance which melts at 154° agrees very well with those obtained in the preceding experiment, and with others for both isomers obtained by Mr. G. H. Shadinger.

All of the above evidence seems to bear out the conclusion that these 2 modifications of the carbethoxyphenylsemicarbazide are not chemical isomers, but are some kind of physical isomers. As soon as time permits, the subject will be taken up again. Analysis:

I. 0.2168 gram substance (m. p. 172°) gave 43.1 cc. N at 18° and 635 mm.

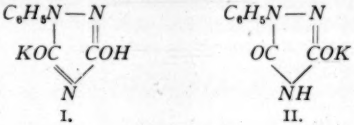
II. 0.0901 gram substance (m. p. 154°) gave 17.8 cc. N at 18° and 633 mm.

	Calculated for $C_{10}H_{12}O_3N_2$.	Found. I.	II.
N	18.83	19.16	18.98

Potassium Phenylsemicarbazide-a-carboxylate,[1] $C_6H_5N(COOK)NHCONH_2$. — When carbethoxyphenylsemicarbazide is heated in aqueous solution with a molecular amount

[1] Acree: Ber. d. chem. Ges., **37**, 621.

of potassium hydroxide and a drop of phenolphthalein, till the red color disappears, the above potassium salt can be obtained by evaporating the solution to crystallization. When the residue is washed with alcohol and ether, the salt is pure and white. When the salt is treated in aqueous solution with hydrochloric acid, pure phenylurazole is formed. When the salt is heated at 150° it loses a molecule of water and gives potassium phenylurazole, formula I. or II.,



which gives pure phenylurazole when treated with hydrochloric acid. Analysis:

0.2598 gram substance lost 0.0215 gram H_2O when heated 3 hours at 120°–150°; 0.1586 gram dried substance gave 0.0640 gram K_2SO_4.

	Calculated for $C_8H_6O_2N_3K$.	Found.
H_2O	7.72	8.24

	Calculated for $C_8H_6O_2N_3K$.	Found.
K	18.18	18.12

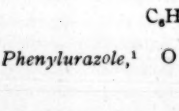
Silver Phenylsemicarbazide-α-carboxylate,[1] $C_6H_5N(COOAg)NHCONH_2$.—When a solution of potassium phenylsemicarbazide-α-carboxylate is titrated with the theoretical amount of silver nitrate solution, with stirring, the silver salt comes out as a granular precipitate. When the salt is heated to 150° it loses 1 molecule of water and gives silver phenylurazole, I. or II. Analysis:

I. 0.1532 gram substance gave 0.0557 gram Ag.

II. 0.2084 gram substance (dried at 150°) gave 0.0801 gram Ag.

[1] Acree: Ber. d. Chem. Ges., **37**, 622, 995.

Calculated for	Ag.	Found.
$C_8H_9O_3N_2Ag$	35.72	36.36
$C_8H_6O_2N_2Ag$	38.00	38.44

Phenylurazole,[1]  —This compound[2] is most easily obtained by heating the carbethoxyphenylsemicarbazide with a molecule of alkali till the ester is saponified, and treating the resulting solution with an excess of a mineral acid. The phenylsemicarbazidecarboxylic acid,

$$C_6H_5N(COOH)NHCONH_2,$$

is first liberated, but loses a molecule of water at once and forms phenylurazole.

Phenylurazole reddens litmus and decomposes carbonates. In the presence of phenolphthalein or Poirrier's Blue, phenylurazole titrates against only 1 molecule of alkali. Since the Porrier's Blue is very sensitive to hydrogen ions, it is clear that the 4,5-amide group in sodium phenylurazole gives only a very small amount of hydrogen ions. The alkali salts color methyl orange brown; in these solutions the metal can be estimated quantitatively by titration with standard hydrochloric acid. Insoluble salts are formed when solutions of the alkali salts of phenylurazole are treated with solutions of silver nitrate, copper sulphate, mercuric chloride, lead chloride, and others.

When potassium phenylurazole is warmed with an iodine solution the iodine gradually reacts with the salt and an organic compound is formed which is very soluble in water. This is now being investigated.

When potassium phenylurazole is boiled in alcoholic-water solutions with alkyl halides, the 1-phenyl-2-*N*-alkylurazoles are formed, together with small quantities of the 1-phenyl-3-

[1] The graphic formula given with the name of the substance represents the particular tautomeric form supposed to be present in greatest amount in solutions of the substance.

[2] Acree: This Journal, **27**, 118; **31**, 185; **32**, 606; **37**, 71. Ber. d. chem. Ges., **35**, 553; **36**, 3139; **37**, 184, 618.

alkoxyurazoles and others. Not only has the 1-phenyl-2-methylurazole been made, but Mr. R. F. Brunel, who is working on the urazoles, has found the method admirably adapted to the formation of the corresponding 2-ethyl, -propyl, -isopropyl, -butyl, -isobutyl, -tertbutyl, and -isoamyl derivatives, and will report his work later. When the silver salt is treated with the corresponding alkyl halides a comparatively large amount of the 1-phenyl-3-alkoxyurazole is formed.

When phenylurazole is treated with an excess of diazomethane[1] the chief product is 1-phenyl-3-methoxy-4-methylurazole. When an alcoholic hydrochloric acid solution of this dimethyl derivative is boiled some time, the methoxy group at 3- is saponified and 1-phenyl-4-methylurazole is formed. When a solution of diazomethane is added to an excess of phenylurazole, the chief reaction product is 1-phenyl-3-methoxyurazole, together with a small amount of 1-phenyl-2-methylurazole. When the 1-phenyl-3-methoxyurazole is boiled with alcoholic hydrochloric acid, the methoxy group is saponified and phenylurazole is formed. These facts, then, show that phenylurazole reacts toward diazomethane as if it has an enol group at 3 and a hydrogen on the N at 4.

Conductivity measurements on all of these urazoles, as well as on the salts, are being conducted now by Mr. G. H. Shadinger and the writer. The strength of the acid groups at 2,3- and 4,5- in the various compounds, together with a study of all the conditions affecting the strength of these acids, are being very minutely investigated. The 2,3-amide group in phenylurazole has an affinity constant $K = 0.00001$ at 25°, whereas the 4,5-amide group has a constant $K = 0.00000005$. These acids obey Ostwald's dilution law and we shall study their conductivities, and those of their salts, at other temperatures to get the temperature coefficients of their conductivities and their dissociation constants and to see if changes in temperature affect the value of the Ostwald constant or the tautomeric relations.

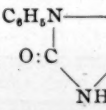
Phenyldibenzoylurazole.—Silver phenylurazole, 7.7 grams, was allowed to stand 2 months with 3.9 grams of benzoyl

[1] Acree: Ber. d. chem. Ges., **36**, 3139.

chloride in benzene solution. The liquid was filtered from the silver chloride and evaporated in a desiccator over paraffin. A solid, melting at 178°–180°, was obtained, which is the dibenzoyl derivative. It is rather surprising that the dibenzoyl derivative is the only product obtained, when we recall that in the corresponding experiment with acetyl chloride[1] very little diacetyl and much monoacetyl derivative is formed. Analysis:

0.1525 gram substance gave 17.5 cc. N at 22° and 630 mm.

	Calculated for $C_{23}H_{15}N_3O_3$.	Found.
N	10.93	10.77

Potassium Phenylurazole,  —Mr. Ralph Watson, of the University of Utah, made this salt by neutralizing phenylurazole with exactly 1 molecule of potassium hydroxide in aqueous solution and evaporating the solution on a water-bath just to dryness. The salt was then washed with alcohol and ether. It contains, in this state, no water of crystallization. The salt can be crystallized very nicely from a concentrated water solution by cooling, or by the addition of alcohol. The salt is difficultly soluble in alcohol. When a water solution of the salt is treated with hydrochloric acid pure phenylurazole is regenerated. Analysis:

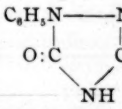
1.03554 grams substance lost 0.0075 gram H_2O when heated 3 hours, at 140°.

I. 0.1560 gram dried salt required 6.45 cc. 0.1125 N hydrochloric acid (indicator: methyl orange).

II. 0.7635 gram salt gave 0.3092 gram K_2SO_4.

	Calculated for $C_9H_6N_3O_3K$.	Found.	
		I.	II.
K	18.18	18.21	18.19

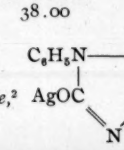
[1] Acree: This Journal, **32**, 609. Wheeler and Johnson: *Ibid.*, **30**, 24.



Silver Phenylurazole,[1] $C_6H_5N{-}{-}N$ / $O{:}C$ ‖ $COAg$ / NH.—When a solution of potassium phenylurazole is treated with a standard silver nitrate solution, the silver phenylurazole first formed redissolves; after 0.5 gram molecule of silver nitrate has been added, however, a permanent precipitate is formed upon the addition of the second half of the silver nitrate, the amount being nearly the theoretical. This seems to show that a soluble alkali-silver double salt is first formed in the titration. When the precipitated silver salt is filtered off and washed well with water, alcohol and ether, it is pure white and very stable towards light. That the silver is mostly at 3- is made probable by the fact that ethyl iodide and the silver salt give 1-phenyl-3-ethoxyurazole, while acetyl chloride and the silver salt give the corresponding 1-phenyl-2- or -3-acetylurazole. Analysis:

0.2143 gram substance gave 0.0816 gram Ag.

	Calculated for $C_8H_6N_2O_2Ag$.	Found.
Ag	38.00	38.08



Disilver Phenylurazole,[2] $C_6H_5N{-}{-}N$ / $AgOC$ ‖ $COAg$ / N.—When a solution of sodium phenylurazole and phenolphthalein is treated with a measured volume of 0.1 N sodium hydroxide solution, less than 1 molecule, just twice this volume of 0.1 N silver nitrate must be added to make the red color of the solution disappear; or if a measured volume of 0.1 N silver nitrate solution is added to the solution, just half this volume of 0.1 N alkali is sufficient to bring back the red color. When silver phenylurazole, in the presence of phenolphthalein, is treated alternately with 0.1 N alkali solution and 0.1 N silver nitrate

[1] Acree: THIS JOURNAL, **27**, 128; **31**, 185; **33**, 606. Ber. d. chem. Ges., **35**, 553; **36**, 3139; **37**, 618.

[2] Acree: *Ibid.*, **36**, 3146.

solution, it requires the same volume of silver nitrate solution to remove the red color as of alkali solution to produce that color. The precipitate formed is disilver phenylurazole. Phenylurazole is easily converted into its disilver salt, then, by dissolving it in 0.1 N alkali and treating it alternately with 0.1 N alkali and 0.1 N silver nitrate until 2 molecules each of the alkali and the silver nitrate have been used. The solution should be dilute and should be shaken thoroughly during the operation; otherwise the disilver salt precipitates out as a jelly-like mass, which is hard to filter. The yield is practically quantitative. In one experiment, for example, 16 grams of phenylurazole gave 35 grams of disilver salt instead of the theoretical amount of 35.5 grams: in another experiment 5 grams of phenylurazole gave 11 grams of the disilver salt instead of 11.05 grams. When freshly precipitated, the salt is light gray but soon becomes dark brown. During this change of color no perceptible decomposition takes place; a sample of the salt stood 2 months in a desiccator and was analyzed from time to time. It contained the theoretical amount of silver. When this disilver salt is treated with ethyl iodide in benzene or ether solution, nearly pure 1-phenyl-3,5-diethoxyurazole (m. p. 53°) is formed. Mr. R. F. Brunel is using the same method for the preparation of other homologues. Analysis:

I. 0.1399 gram substance gave 0.0763 gram Ag.
II. 0.2113 gram substance gave 0.1171 gram Ag.
III. 0.2237 gram substance gave 0.1213 gram Ag.
IV. 0.2340 gram substance gave 0.1240 gram Ag.
V. 0.2492 gram substance gave 0.1354 gram Ag.
VI. 0.2056 gram substance gave 0.1141 gram Ag.

III., IV. and V. are analyses, made at intervals, of a sample that stood 1 month in a desiccator.

	Calculated for $C_8H_8N_2O_2Ag_2$.	Found.					
		I	II.	III.	IV.	V.	VI.
Ag	55.20	54.54	55.42	54.23	53.00	54.37	55.50

The study of the method of formation of this disilver salt and the corresponding disilver 1-phenyl-3-thiourazole has given some valuable data concerning the ionization of phenylurazole and its salts. Two questions can now be answered. First,

when a fraction of a molecular quantity of potassium hydroxide is added to a solution of a molecular quantity of potassium phenylurazole, is the potassium phenylurazole a strong enough acid to unite with this alkali completely, or nearly so, or does the alkali remain practically undiminished in quantity? In other words, is dipotassium phenylurazole, in water solution, greatly hydrolyzed into potassium hydroxide and potassium phenylurazole or only slightly so? The experiments show that when a solution of potassium phenylurazole is treated with a further quantity of alkali, the alkali reacts nearly completely with the potassium phenylurazole and gives dipotassium phenylurazole, and there is only a small amount of free alkali left in the solution. As a result, when the silver nitrate is added it reacts immediately with the dipotassium phenylurazole present and forms the insoluble disilver salt, and the small amount of free alkali present simultaneously reacts with some of the potassium phenylurazole to form more dipotassum phenylurazole. If there were much free alkali present in the solution at any time the silver nitrate would react with this to form silver oxide and as a result the precipitate would contain a much higher percentage of silver than that corresponding to disilver phenylurazole. Since the analytical data show the disilver phenylurazole to be pure, there is no silver oxide in it, and consequently there is very little free alkali present in a solution of potassium phenylurazole and a fraction of a molecular quantity of alkali. McCoy[1] found that in 0.05 gram molecular solutions the hydrolysis of sodium carbonate into sodium hydroxide and sodium bicarbonate is only 6.2 per cent. Judging from the affinity constants of phenylurazole and of carbonic acid, potassium phenylurazole is a stronger acid than sodium bicarbonate and dipotassium phenylurazole is probably not hydrolyzed as much as 6 per cent.

The second question answered by the experiments is: Is silver phenylurazole a strong enough acid to titrate against a measurable amount of 0.1 N alkali in the presence of phenolphthalein, without appreciably sharing the alkali with the

[1] This Journal, **29**, 462.

phenolphthalein and causing a red coloration of the solution? In the discussion of the ionization of the acid salts of phenylurazole it suggests itself that if we could prepare phenyl acid urazole salts (XXIII.), in which the dissociation into metal ions and phenylurazole ions is small in comparison with that of the alkali salts, we should then have compounds which should be more acid than the alkali salts and in which 4,5-amide group would titrate against some alkali without sharing it perceptibly with the phenolphthalein, just as do the phenyl-3-alkoxyurazoles. Since silver salts, in general, are less ionized than the corresponding alkali salts, silver phenylurazole was investigated to see if it would show this behavior. Careful experiments made us doubt that silver phenylurazole is more acid than potassium phenylurazole.

A number of series of experiments were carried out to test this point in question, but only one representative series will be given here. The largest experimental error is that one due probably to the failure of the reagent added to mix thoroughly and quickly with the gelatinous solution containing the precipitated silver salt. It was found, furthermore, that it takes from 0.08 to 0.15 cc. 0.1 N potassium hydroxide to give a decisive red color in a solution containing 5 cc. 0.1 N silver nitrate, 50 cc. of water and some phenolphthalein. It is probable, then, that the experimental error in these determinations may be as high as 0.20 cc. in the more concentrated solutions. In some titrations less than 1 molecular quantity of 0.1 N silver nitrate solution was added to the potassium phenylurazole solution, in other cases more than a molecular quantity was added; then alkali was added till the red color appeared. In other cases 1 molecular quantity of 0.1 N silver nitrate solution was added to the potassium phenylurazole solution; to the precipitated silver salt was then added a measured volume of 0.1 N potassium hydroxide (1 or 2 drops of alkali will color the solution red) and then sufficient 0.1 N silver nitrate solution just to remove the pink color. But whatever the method of procedure used, when we start with a given amount of potassium phenylurazole the volume of 0.1 N silver nitrate solution necessary to remove the red color is just

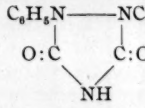
twice the volume of the 0.1 N alkali added. The precipitate is the disilver phenylurazole. The figures show that the silver phenylurazole does not titrate against an amount of 0.1 N alkali greater than that involved in the experimental error. A similar series of determinations was made with phenyl-3-thiourazole, and the result was the same; 0.1000 gram of phenylurazole required 5.65 cc. 0.1 N of potassium hydroxide in 50 cc. water and phenolphthalein. Calculated, 5.65 cc.

To this solution was added the following volumes of 0.1 N potassium hydroxide and 0.1 N silver nitrate to keep the solution neutral to phenolphthalein.

0.1 N KOH.	0.1 N $AgNO_3$.
cc.	cc.
0.28	0.60
1.03	2.19
2.12	4.18
2.90	5.58
3.20	5.98
4.31	7.97
5.65	11.24
(5.61)	(11.26)

An examination of the column on the left, representing the amount of alkali needed to render the solution neutral to phenolphthalein, shows that in some cases there is considerable more than half the corresponding volume of 0.1 N silver nitrate; in other words, the silver phenylurazole seems to titrate against some of the alkali before beginning to share it perceptibly with the phenolphthalein. But the experimental error of the titrations is so large that such a conclusion is hardly justified. More refined work, however, will be undertaken.

Phenyl-2-methylurazole,[1]



.—This substance was first made by Busch by the elimination of the amino group from phenyl-2-methyl-4-aminourazole by means of nitrous

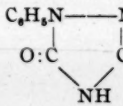
[1] Busch and Heinrichs: Ber. d. chem. Ges., **33**, 455. Acree: This Journal, **27**, 128.

acid. Busch supposed the methyl group to be in position 3, but this formula was proved by the writer to be incorrect. The substance was obtained by the writer by the action of methyl iodide on potassium phenylurazole, and it has been found by Mr. R. F. Brunel that this method is a general one for the preparation of phenyl-2-alkylurazoles, a small amount of the corresponding phenyl-3-alkoxyurazole being formed at the same time in this reaction.

This substance has now been prepared by the action of dimethyl sulphate on potassium phenylurazole, and by the action of diazomethane on phenylurazole.

Ten grams of phenylurazole dissolved in 1 molecular quantity of potassium hydroxide in water, was treated with 1.25 mol. of dimethyl sulphate and shaken well; some alkali was added at intervals. A precipitate was formed which, when dried and extracted with chloroform, gave 4.75 grams of phenyl-2-methylurazole, not quite pure. This was dissolved in alkali and fractionally precipitated by adding sulphuric acid. One fraction, 3 grams, melted at 170°–182°, and the other, 1.5 grams, at 185°–188°. The melting point of this latter fraction was not lowered by mixing it with pure 1-phenyl-2-methylurazole. One gram required 5.55 cc. 0.907 N potassium hydroxide (indicator, phenolphthalein); calculated, 5.75 cc.

Phenyl-3-methoxyurazole,[1]



—The action of diazomethane on the urazoles in ether solution was studied to learn the position of the hydrogen atoms in the non-ionized substances. The 2,3- and the 4,5-amide groups contain the 2 tautomeric forms

$$—NHCO— \rightleftharpoons —N:C(OH)—$$

in equilibrium with each other, and only traces of their ions. Since diazomethane reacts very readily with imido and with enol groups, the determination of the relative amounts of

[1] Acree: Ber. d. chem. Ges., **36**, 3150.

N-methyl and of methoxy derivatives formed would give us some knowledge of the ratio in which the 2 tautomeric forms exist in the ether. Although diazomethane reacts practically instantaneously with these urazoles, yet it may be that one of the 2 forms, the enol or the keto, reacts with the diazomethane a little more readily than does the other form. In this case, the above equation of equilibrium would not hold exactly; the change in equilibrium would take place in the direction of the form more readily acted upon by the diazomethane, and as a consequence, more of that particular methylated product would be obtained than would be expected from the above equation of equilibrium. But the results obtained give us, probably, fairly accurately the ratios in which the 2 forms exist and the data so obtained are valuable and instructive and harmonize with the evidence secured by physical-chemical means by Mr. Shadinger.

When an absolute ether solution of diazomethane was allowed to drop into a vessel containing solid phenylurazole and the mixture was shaken well, the diazomethane was decomposed at once. The ether solution was filtered, evaporated to dryness and extracted with chloroform to leave undissolved any unchanged phenylurazole. The chloroform was evaporated and the residue was dissolved in a small amount of alcohol. To this solution was added phenolphthalein, a small excess of alkali and several volumes of water, in order to remove the insoluble 1-phenyl-3-methoxy-4-methylurazole, which will be described below. The precipitate was filtered off and the filtrate was evaporated to a small volume. Hydrochloric acid was added to the cooled solution, and a copious precipitate of 1-phenyl-3-methoxyurazole was formed and was filtered off. The filtrate contained a small amount of 1-phenyl-2-methylurazole; when the solution was evaporated to dryness and the residue was crystallized from a small amount of hot water the substance was obtained pure, melting at 183°. Titration: 0.1131 gram required 5.88 cc. 0.1 N potassium hydroxide solution; calculated, 5.92 cc.

1-phenyl-3-methoxyurazole melts at 197°, undecomposed. It titrates against 0.1 N alkali as a monobasic acid and is pre-

cipitated unchanged from the alkaline solution upon the addition of strong acids. The monopotassium salt was analyzed. When evaporated on a water-bath 2 or 3 times with concentrated alcoholic hydrochloric acid, the 1-phenyl-3-methoxyurazole is changed into pure phenylurazole, which melts at 263°–265°.

That the methoxy group is at 3- and not at 5- was proved by the fact that further methylation, by means of diazomethane, gives 1-phenyl-3-methoxy-4-methylurazole, which melts at 95°–96°. This proves, too, that the hydrogen of the 1-phenyl-3-methoxyurazole is chiefly at 4- and not at 5-. When the sodium salt of 1-phenyl-3-methoxyurazole is heated, in alcoholic solution, with methyl iodide, at 100°, the same 1-phenyl-3-methoxy-4-methylurazole, melting at 95°–96°, is formed. A mixture of samples of the 1-phenyl-3-methoxy-4-methylurazole, prepared by the 2 methods, melts at 95°–96°, and when either sample is evaporated with alcoholic hydrochloric acid, the methoxy group at 3- is saponified and 1-phenyl-4-methylurazole, melting at 223°, is obtained.

Titration: (1) 0.2482 gram substance required 13.8 cc. 0.0937 N sodium hydroxide; calculated, 13.87 cc. (2) 0.1075 gram substance required 6.20 cc. 0.08943 N sodium hydroxide; calculated, 6.29 cc. Analysis:

0.0542 gram substance gave 12.8 cc. N at 18° and 628 mm.

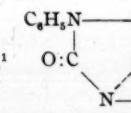
	Calculated for $C_9H_9N_3O_2$.	Found.
N	22.02	22.52

Potassium Phenyl-3-methoxyurazole, $C_9H_8N_3O_2K.H_2O$.—This salt was made by titrating 1-phenyl-3-methoxyurazole with a molecular proportion of 0.1 N potassium hydroxide and evaporating the solution to dryness. When a solution of the salt was treated with hydrochloric acid, the 1-phenyl-3-methoxyurazole precipitated out unchanged, melting at 197°. Analysis:

0.1431 gram substance, dried 24 hours in a vacuum, over sulphuric acid, lost 0.0108 gram H_2O when heated 2 hours at 135°, and the residue required 6.15 cc. of 0.09743 N hydrochloric acid, with methyl orange.

	Calculated for $C_9H_8N_3O_2K.H_2O$.	Found.
H_2O	7.28	7.55
K	16.92	16.40

1-Phenyl-4-methylurazole,[1]



—This methyl derivative was first made by the writer by heating phenylsemicarbazide and methylacetylurea together at 200°. The yield was about 20 per cent, but the substance can now be made nearly quantitatively by heating any of the following compounds with hydrochloric acid: 1-Phenyl-3-methoxy-4-methylurazole, 1-phenyl-3-ethoxy-4-methylurazole, or 1-phenyl(2 or 3)acetyl-4-methylurazole. This methyl derivative can be made best in large quantities by boiling potassium 1-phenyl-4-methyl-5-thiourazole with methyl iodide in 50 per cent alcohol. The samples of 1-phenyl-4-methylurazole prepared from these substances all melt at 223°–225°, and mixtures melt at the same temperature. The substance is soluble in benzene and chloroform and can be easily separated from phenylurazole by means of these solvents. It can be crystallized very nicely from alcohol or water.

The 1-phenyl-3-ethoxy-4-methylurazole can be made very easily by boiling the sodium salt of 1-phenyl-3-ethoxyurazole with methyl iodide, in alcoholic water solution, or by shaking the salt in water solution with dimethyl sulphate. Mr. Brunel has found that these methods can be used with advantage for the preparation of other 4-alkyl homologues, and that these 1-phenyl-3-ethoxy-4-alkylurazoles yield the corresponding 1-phenyl-4-alkylurazoles when hydrolyzed with hydrochloric acid. Analysis:

I. 0.1284 gram substance gave 28.2 cc. N at 17° and 636 mm.

II. 0.0993 gram substance gave 22.8 cc. N at 19°.5 and 631 mm.

III. 0.1312 gram substance gave 33 cc. N at 32° and 613 mm.

[1] Acree: This Journal, **27**, 130; Ber. d. chem. Ges., **38**, 3149.

IV. 0.1376 gram substance gave 34.5 cc. N at 32° and 614 mm.

	Calculated for $C_9H_9N_3O_2$.	Found. I.	II.	III.	IV.
N	22.02	21.30	21.84	21.74	21.70

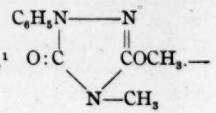
These analyses were made with preparations of the following origin: (1) 1-Phenyl-3-acetyl-4-methylurazole, m. p. 94°, and hydrochloric acid. (II.) 1-Phenyl-3-acetyl-4-methylurazole, m. p. 94°, and potassium hydroxide. (III.) Hydrochloric acid and 1-phenyl-3-ethoxy-4-methylurazole formed from methyl iodide and sodium 1-phenyl-3-ethoxyurazole. (IV.) Hydrochloric acid and 1-phenyl-3-ethoxy-4-methylurazole prepared by the interaction of diazomethane and 1-phenyl-3-ethoxyurazole.

1-Phenyl-2-benzoyl-4-methylurazole, $C_9H_8N_3O_2COC_6H_5$. — A small amount of 1-phenyl-4-methylurazole was neutralized with potassium hydroxide, treated with the calculated amount of benzoyl chloride and shaken vigorously. The benzoyl derivative precipitated out at once and when dry melted at 185°. It is readily soluble in ether and alcohol, but insoluble in water. When it was warmed with concentrated hydrochloric acid, the pure 1-phenyl-4-methylurazole was formed by hydrolysis. Analysis:

0.1302 gram substance gave 15.75 cc. N at 13° and 744.1 mm.

	Calculated for $C_{16}H_{13}N_3O_2$.	Found.
N	14.27	14.04

1-Phenyl-3-methoxy-4-methylurazole,[1]



This substance was obtained very easily by adding solid phenylurazole slowly to an absolute ether solution of diazomethane. When the diazomethane was all used up, which was recognized by the disappearance of the yellow color of the solution, the ether was distilled off, the residue dissolved in alcohol and

[1] Acree: Ber. d. chem. Ges., **38**, 3149.

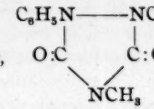
the solution was made slightly alkaline. Water was added to the solution till it became turbid. When it was cooled, 1-phenyl-3-methoxy-4-methylurazole precipitated out in needles and more of the same substance was extracted from the liquid by means of ether. It melted at 95°. When the substance was evaporated with alcoholic hydrochloric acid, 1-phenyl-4-methylurazole, which melted at 223°, was formed. This experiment shows that phenylurazole, in ether solution, probably has the hydrogens chiefly at 3- and 4-. A mixture of this 1-phenyl-3-methoxy-4-methylurazole and 1-phenyl-3-ethoxy-4-methylurazole, which melts at 95°–96°, melted at 75°–78°.

1-Phenyl-3-methoxyurazole, 0.2482 gram, m. p. 194°, titrated in alcohol against 13.80 cc. 0.0937 N sodium hydroxide solution (calculated, 13.87 cc.). Methyl iodide was added and this solution was boiled several hours under a return condenser. The solution was then evaporated to dryness, taken up in alcohol, made alkaline, and cooled. When water was added slowly a precipitate of 1-phenyl-3-methoxy-4-methylurazole, which melted at 95°-96°, was formed. A mixture of this substance and the one described above, melted at 95°. When this substance was evaporated several times with alcoholic hydrochloric acid, 1-phenyl-4-methylurazole, which melted at 223°, was formed. Analysis:

0.0818 gram substance, made from diazomethane and phenylurazole, gave 17.4 cc. N at 19° and 634 mm.

	Calculated for $C_{10}H_{11}N_3O_2$.	Found.
N	20.52	20.38

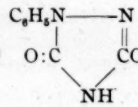
1-Phenyl-2,4-dimethylurazole,



.—To 1 gram phenylurazole, in a stoppered bottle, was added an excess of potassium hydroxide solution and 5 grams of neutral dimethyl sulphate. The mixture was shaken several hours in a machine till the dimethyl sulphate disappeared. Small quantities of alkali were added from time to time to keep the solution

slightly alkaline. The precipitate of the dimethyl derivative was filtered and dried. When crystallized from ligroin it melted at 95° and is probably identical with the products obtained by Pinner[1] and by Busch[2] by the methylation of phenylurazole alkali salts by means of methyl iodide. When evaporated repeatedly with alcoholic hydrochloric acid, there was no change in the melting point.

1-Phenyl-3-ethoxyurazole,[3]



—This substance was formed together with 1-phenyl-3,5-diethoxyurazole, phenylurazole, and probably some *N*-ethyl derivatives, when silver phenylurazole was treated with ethyl iodide in cold or boiling ether, or in cold benzene solution. It is more convenient to have some glass beads in the flask containing the solution, as the silver salts can then be kept finely divided, and the reaction can be ended in 2 or 3 days. The reaction is never complete. The solution was filtered and the residue of the silver iodide was extracted 2 or 3 times with small quantities of warm ether, benzene, or chloroform, and these extracts were added to the first filtrate. This solution was then evaporated to dryness, the residue was dissolved in a small volume of hot alcohol and phenolphthalein was added; upon the addition of an excess of alkali and considerable water, 1-phenyl-3,5-diethoxyurazole, which melted at 53°, was obtained as a precipitate and a small amount more was then extracted from the alkaline solution by means of ether. When the alkaline solution was warmed to remove the ether and was treated with a slight excess of sulphuric acid, a precipitate of impure 1-phenyl-3-ethoxyurazole was formed, and more was obtained from the solution by extraction with ether. When the impure 1-phenyl-3-ethoxyurazole was crystallized from 50 per cent alcohol it came out in needles, which melted at 151°–152°. Phenylurazole was obtained by extracting

[1] Ber. d. chem. Ges., **21**, 1223.
[2] *Ibid.*, **35**, 1563.
[3] Acree: This Journal, **27**, 131; **31**, 185; **32**, 606. Ber. d. chem. Ges., **36**, 3146.

the silver iodide residue with hot ethyl alcohol. Other suitable means of separating these compounds have been used.

This 1-phenyl-3-ethoxyurazole is identical with that made by Wheeler. Both melt at 152°, and a mixture melts at the same temperature. Wheeler's method is far better for the preparation of small quantities of the substance. The compound is a monobasic acid and is neutralized by 1 molecular proportion of alkali, in the presence of phenolphthalein. It forms a monosilver salt. When evaporated with alcoholic hydrochloric acid it gives pure phenylurazole. In this reaction ethyl chloride is formed in large quantities, as is also the case when any of the other ethoxyurazoles are treated with gaseous hydrogen chloride, or with hydrochloric acid in alcohol or water solution. We are attempting to use this reaction quantitatively in studying the hydrolysis of the ethoxyurazoles by hydrochloric acid.

When silver 1-phenyl-3-ethoxyurazole is treated with ethyl iodide in ether solution, 1-phenyl-3,5-diethoxyurazole, which melts at 53°, is formed. Through this reaction we obtain light on the rather unexpected formation of phenylurazole and 1-phenyl-3,5-diethoxyurazole in the preparation of 1-phenyl-3-ethoxyurazole from silver phenylurazole and ethyl iodide. Since the 1-phenyl-3-ethoxyurazole is a fairly strong acid, part of it reacts with some of the silver phenylurazole, forming phenylurazole and silver 1-phenyl-3-ethoxyurazole, and this silver salt then reacts with ethyl iodide and forms 1-phenyl-3,5-diethoxyurazole.

When the alkali salts of 1-phenyl-3-ethoxyurazole are boiled several hours, in alcohol solution, with methyl iodide, 1-phenyl-3-ethoxy-4-methylurazole, which melts at 95°, is formed. This gives us, for the first time, proof that Wheeler's ethylated phenylurazole is the 3-ethoxy derivative and not the 5-ethoxy derivative.

When this 1-phenyl-3-ethoxyurazole is treated with diazomethane in ether solution, the same 1-phenyl-3-ethoxy-4-methylurazole, which melts at 95°, is formed. This shows that the active hydrogen atom of the 3-ethoxy compound is probably chiefly at position 4. Titration and analyses:

0.1000 gram substance, made from silver phenylurazole, required 5.45 cc. 0.08943 N potassium hydroxide (indicator, phenolphthalein); calculated, 5.46 cc.

0.5000 gram substance, made by Wheeler's method, required 25.90 cc. 0.0937 N sodium hydroxide; calculated, 26.13 cc.

I. 0.1128 gram substance, made from silver phenylurazole, gave 23.4 cc. N at 13° and 634 mm.

II. 0.1463 gram substance, made by Wheeler's method, gave 34.6 cc. N at 29° and 620 mm.

	Calculated for $C_{10}H_{11}N_3O_2$.	Found. I.	Found. II.
N	20.53	20.44	21.02

Potassium 1-Phenyl-3-ethoxyurazole, $C_{10}H_{10}N_3O_2K.2H_2O$.—This salt was prepared by titrating 1-phenyl-3-ethoxyurazole made by Acree's method, with a molecular quantity of potassium hydroxide and allowing the solution to evaporate to dryness in a desiccator. The water of crystallization was easily expelled by heating the substance at 135°. When a solution of the salt was treated with sulphuric acid, a precipitate of 1-phenyl-3-ethoxyurazole, which melted at 151°, was obtained.

When this salt was boiled in dilute alcoholic solution, with methyl iodide, 1-phenyl-3-ethoxy-4-methylurazole was formed.

When a water solution of this salt was treated with a molecular quantity of silver nitrate, the corresponding silver salt was formed. Analysis:

0.1393 gram substance, heated 2 hours at 135°, lost 0.0182 gram H_2O, and the residue required 5.00 cc. 0.1004 N sulphuric acid (indicator, methyl orange) to give a pink color.

	Calculated for $C_{10}H_{10}N_3O_2K.2H_2O$.	Found.
H_2O	12.90	13.06
K	14.01	14.11

Silver Phenyl-3-ethoxyurazole, $C_{10}H_{10}N_3O_2Ag.H_2O$.—This salt was made as follows: One gram of 1-phenyl-3-ethoxyurazole, made by Wheeler's method, was titrated with the requisite amount of sodium hydroxide solution to give a red color in the

presence of phenolphthalein; when a solution of 0.9 gram of silver nitrate, in water, was added slowly, with stirring, to this solution, the silver salt precipitated out as a light yellow powder. This was filtered off, washed well with water, and allowed to dry on a clay plate. The salt has a molecule of water of crystallization, which is easily expelled at 120°.

When the dry silver salt is treated with ethyl iodide, in ether solution, 1-phenyl-3,5-diethoxyurazole, which melts at 52°, is formed. Analysis:

I. 0.1585 gram substance gave 0.0525 gram Ag.

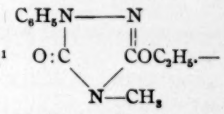
II. 0.1516 gram substance gave 0.0501 gram Ag.

III. 0.1539 gram substance, dried at 120°, gave 0.0526 gram Ag.

	Calculated for $C_{10}H_{10}N_2O_2Ag.H_2O$.	Found. I.	II.
Ag	32.68	33.12	33.05

	Calculated for $C_{10}H_{10}N_2O_2Ag$.	Found. III.
Ag	34.58	34.18

1-Phenyl-3-ethoxy-4-methylurazole,[1]



I. A half gram of 1-phenyl-3-ethoxyurazole, in alcohol, was titrated with 25.90 cc. 0.0937 N sodium hydroxide, in the presence of phenolphthalein (calculated, 26.13 cc.), and 1 gram of methyl iodide was added to the solution. The mixture was boiled under a return condenser for 6 hours and small amounts of potassium hydroxide solution and methyl iodide were added from time to time. The solution was evaporated to dryness, the residue was treated with water and filtered and 0.45 gram of 1-phenyl-3-ethoxy-4-methylurazole was obtained as a solid insoluble in water. When recrystallized from 50 per cent alcohol, containing a small amount of alkali, the substance was obtained in fine leaflets, that melted at 95°–96°. When mixed with a sample of the substance, which melted at 94°, made by the action of diazo-

[1] Acree: Ber. d. chem. Ges., **36**, 3148.

methane on 1-phenyl-3-ethoxyurazole, the mixture melted at 94°–95°. A sample of the substance was evaporated with alcoholic hydrochloric acid for 1 hour and was converted into the 1-phenyl-4-methylurazole, which melted at 223°–224°. The compound is soluble in nearly all of the organic solvents, but insoluble in water. This experiment has been repeated several times with the same results, whether Acree's or Wheeler's 1-phenyl-3-ethoxyurazole is used.

II. To 0.5 gram phenyl-3-ethoxyurazole was added slightly more than enough alkali to neutralize the urazole, and then 5 grams of neutral dimethyl sulphate. The bottle was shaken 3 hours in a shaking machine and small portions of alkali were added intermittently to keep the solution always slightly alkaline. At the end of this time all of the dimethyl sulphate had been used up and a granular precipitate of 1-phenyl-3-ethoxy-4-methylurazole was obtained. This melted, without recrystallization, at 95°–96°, and at the same temperature when mixed with a sample made by Method I. The substance is soluble in dimethyl sulphate. A yield of 0.52 gram was obtained, which is nearly the theoretical. This method has been used a number of times for preparing 1-phenyl-3-ethoxy-4-methylurazole in large quantities and has proved to be very satisfactory.

III. The action of diazomethane on 1-phenyl-3-ethoxyurazole was studied to try to learn the position of the hydrogen in the urazole ring. Since in the ether solution the urazole is not appreciably ionized, the determination of the ratio of the amounts of the 2 methylation products, namely, 1-phenyl-3-ethoxy-4-methylurazole and 1-phenyl-3-ethoxy-5-methoxyurazole, would give us, probably, approximately, the relative amounts of keto and enol forms, respectively,

$$—NHCO— \rightleftharpoons —N:C(OH)—$$

existing in equilibrium with each other in the 4,5-amide group in 1-phenyl-3-ethoxyurazole. If, for instance, in phenyl-3-ethoxyurazole in ether solution 0.9 of the hydrogen were at 4- (in XVI.), and 0.1 were at 5- in the enol form, and if the 2 forms react equally readily with diazomethane, then we should obtain

by the action of diazomethane on 1-phenyl-3-ethoxyurazole, 9 parts of 1-phenyl-3-ethoxy-4-methylurazole and 1 part of 1-phenyl-3-ethoxy-5-methoxyurazole.

1-Phenyl-3-ethoxyurazole, in ether, was treated with an ether solution of diazomethane. There was a vigorous evolution of nitrogen and the diazomethane was used up at once. The ether was evaporated off, the residue was dissolved in alcohol, made slightly alkaline with potassium hydroxide and the mixture evaporated to dryness. The residue was digested with water to remove the soluble alkali salts and filtered. The 1-phenyl-3-ethoxy-4-methylurazole remaining on the filter was recrystallized from 50 per cent alcohol containing some potassium hydroxide. It was obtained as leaflets, which melted at 94°; when mixed with a sample prepared in the preceding experiments, it melted at 94°–95°. Some of this substance was evaporated twice with concentrated alcoholic hydrochloric acid; the ethoxy group at 3- was saponified and pure 1-phenyl-4-methylurazole, which melted at 223°–224°, was formed. This 1-phenyl-4-methylurazole melted at the same temperature when mixed with a sample prepared by another method. A mixture of this 1-phenyl-3-ethoxy-4-methylurazole, melting at 95°, and 1-phenyl-3-methoxy-4-methylurazole, which melted at 95°, fused at 75°–78°.

The alcoholic filtrate from the above 1-phenyl-3-ethoxy-4-methylurazole was evaporated to dryness, the residue was washed well with water and then evaporated with alcoholic hydrochloric acid. When this residue was extracted with chloroform a very small amount of slightly impure phenylurazole was obtained. A small amount of 1-phenyl-3-ethoxy-5-methylurazole was, therefore, formed in this experiment, and when saponified by hydrochloric acid, it gave the phenylurazole. By the action of diazomethane, then, on phenyl-3-ethoxyurazole, we obtain a large amount of 1-phenyl-3-ethoxy-4-methylurazole and only a very small quantity of 1-phenyl-3-ethoxy-5-methoxyurazole. This shows that in ether solution nearly all of the 1-phenyl-3-ethoxyurazole exists as the keto form with the hydrogen at 4- (XVI.) and only a very small amount of the substance exists in the enol form with the hy-

drogen atom at 5- (I.). The contrast in the behavior of this 4,5-amide group in phenyl-3-ethoxyurazole, 1-phenyl-3-methoxyurazole, 1-phenyl-3-thiomethylurazole, 1-phenyl-2-acetylurazole, phenylurazole and 1-phenyl-3-thiourazole, with the behavior of the 2,3-amide group in phenylurazole and phenyl-3-thiourazole is very striking. Diazomethane converts all the compounds containing the 4,5-amide group chiefly into 4-methyl derivatives, with only a trace of 5-methoxy derivatives. Diazomethane converts all the compounds containing the 2,3-amide group chiefly into 3-methoxy or 3-thiomethyl derivatives, with only a trace of 2-methyl derivatives. The conclusion to be drawn is that the 2,3-amide group reacts toward diazomethane chiefly in the enol form, whereas the 4,5-amide group reacts chiefly as the keto form.

Analysis:

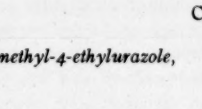
I. 0.1203 gram substance, made by the action of methyl iodide and potassium hydroxide on Wheeler's 1-phenyl-3-ethoxyurazole, gave 26.4 cc. N at 30° and 617 mm.

II. 0.0721 gram substance, made by the action of methyl iodide and sodium hydroxide on Acree's 1-phenyl-3-ethoxyurazole, gave 14.9 cc. N at 22° and 630 mm.

III. 0.1129 gram substance, made by the action of diazomethane on Wheeler's phenyl-3-ethoxyurazole, gave 25 cc. N at 33° and 612 mm.

	Calculated for $C_{11}H_{13}N_3O_2$.	Found. I.	II.	III.
N	19.22	19.31	19.00	19.39

1-Phenyl-2-methyl-4-ethylurazole,

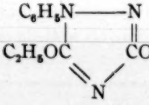


.—To 1 gram 1-phenyl-2-methylurazole, which melted at 185°–188°, was added a drop of phenolphthalein and 5.55 cc. 0.907 N potassium hydroxide (calculated, 5.75 cc.). To this solution was added an equal volume of alcohol and 1 gram of ethyl iodide, and the mixture was boiled for several hours under a return condenser. From time to time a sufficient quantity of alkali

was added to keep the solution slightly alkaline. The mixture was made alkaline and evaporated to dryness and the oily 1-phenyl-2-methyl-4-ethylurazole, which separated out, soon solidified. This solid was filtered from the alkaline solution and crystallized from dilute alcohol made slightly alkaline. It then melted at 113°. When this substance was evaporated twice with concentrated hydrochloric acid, the melting point was not changed, this fact proves that the ethyl group entered at position 4- and not at 3- or 5-. Analysis:

0.0984 gram substance gave 16.1 cc. N at 16° and 773.4 mm. (uncorr.).

	Calculated for $C_{11}H_{13}N_3O_2$.	Found.
N	19.21	19.40

1-Phenyl-3,5-diethoxyurazole,[1]  —It has already been explained that this substance is formed in small quantities in the preparation of phenyl-3-ethoxyurazole from silver phenylurazole and ethyl iodide.

Well dried silver 1-phenyl-3-ethoxyurazole and ethyl iodide, in cold ether solution, stood 3 days. The solution was filtered and the silver iodide mass was extracted 3 times with warm ether. The combined ether solutions were evaporated to dryness. The residue was dissolved in alcohol, filtered, made slightly alkaline with potassium hydroxide, and was treated slowly with an excess of water with vigorous stirring. The mass of fine needles which separated out was filtered off and dried on a clay plate. The substance melted at 52°–53°, whether alone or mixed with samples prepared by the other methods. This method will be used in the attempt to prepare 1-phenyl-3,5-dialkoxyurazoles, in which the 2 alkyl groups are different.

Disilver phenylurazole can be treated with ethyl iodide, in ether solution, or this mixture can be boiled under a return

[1] Acree: THIS JOURNAL, **31**, 185; **32**, 606. Ber. d. chem. Ges., **36**, 3148. Wheeler and Johnson: THIS JOURNAL, **30**, 24.

condenser, during 1 week. The 1-phenyl-3,5-diethoxyurazole was purified in a manner similar to that described in the 2 preceding experiments; it melted at 53°, whether alone or in mixture with the 2 preceding substances. This method gives a yield of 30 to 40 per cent and will be used in an attempt to prepare other 1-phenyl-3,5-dialkoxyurazole homologues.

1-Phenyl-3,5-diethoxyurazole is very soluble in benzene, ether, and alcohol, but insoluble in water. When evaporated with alcoholic hydrochloric acid, pure phenylurazole is formed. The substance possesses magnetic properties to a degree fortunately not often seen in organic substances. If the crystals are pressed out on a clay plate and gently pulverized and are then disturbed with a spatula or a magnet, a great part of the substance flies in all directions, while part adheres very firmly to the spatula or magnet. By stirring the material very gently with the spatula some time, the magnetic properties seem to disappear and the material can be handled without inconvenience. When 1-phenyl-3,5-diethoxyurazole is heated in alcohol, with 1 molecular quantity of hydrochoric acid, the ethoxy group at 5- is saponified and ethyl chloride and 1-phenyl-3-ethoxyurazole are formed, practically quantitatively. This subject will be treated at length in another section. Analysis:

I. 0.1281 gram substance, made by the action of ethyl iodide on silver phenyl-3-ethoxyurazole, gave 26.2 cc. N at 29° and 620 mm.

II. 0.0727 gram substance, made by the action of ethyl iodide on disilver phenylurazole, gave 14.8 cc. N at 28° and 620 mm.

III. 0.1105 gram substance, made by the action of ethyl iodide on silver phenylurazole, gave 20.7 cc. N at 16° and 634 mm.

	Calculated for $C_{12}H_{15}N_3O_2$.	Found.		
		I.	II.	III.
N	18.05	18.19	18.21	18.19

On the Acetyl Derivatives of Phenylurazole: In Conjunction with Mr. Frederick Laist.

In the first publication[1] on the urazoles it was stated that

[1] Acree: THIS JOURNAL, **27**, 118.

when silver phenylurazole was allowed to react with acetyl chloride, in cold benzene, and the solution was filtered, evaporated and dried in a desiccator, an oil was obtained which would not solidify. A nitrogen determination gave 19.35 per cent; calculated for a monoacetyl derivative, N = 19.21 per cent. This oil seemed to be very much more readily hydrolyzed than the 1-phenylacetylurazole, melting at 175°, and was, therefore, thought to be the 1-phenyl-3-oxyacetylurazole, and the acetyl derivative, m. p. 175°, was supposed to be the 1-phenyl-2-acetylurazole. The acetyl group was thought to be in position 2-, rather than 4-, because 2-alkyl derivatives were produced by the alkylation of phenylurazole salts by alkyl halides at high temperatures. The experiment was afterwards repeated[1] and there was obtained chiefly 1-phenylacetylurazole, melting at 175°, together with small amounts of phenyldiacetylurazole and phenylurazole. Shortly before this an article had appeared by Wheeler and Johnson[2] in which they questioned the results of the writer and stated that they obtained by this reaction phenylurazole and a labile phenyldiacetylurazole. The writer then repeated[3] the former experiment and obtained again as the chief reaction product 1-phenylacetylurazole, and small amounts of phenylurazole and phenyldiacetylurazole, but none of the labile diacetyl derivatives described by Wheeler and Johnson.

Mr. Frederick Laist, working under the direction of the writer, in the University of Utah, in continuing these investigations, made some phenylacetylurazole melting at 173°, according to the directions of Cuneo, and treated this with diazomethane. 1-Phenylacetyl-4-methylurazole,[4] melting at 94°, was formed. When this substance was fused it quickly resolidified and was thereby transformed into an isomer, melting at 113°–115°, identical with Busch's[5] 1-phenylacetyl-4-methylurazole, m. p. 113°–115°, made by acetylating 1-phenyl-4-methylurazole. The same rearrangement of the acetyl derivative of

[1] Acree: Ber. d. chem. Ges., **36**, 3143.
[2] This Journal, **30**, 24.
[3] Acree: *Ibid.*, **31**, 185; **32**, 606.
[4] Acree: Ber. d. chem. Ges., **36**, 3143.
[5] *Ibid.*, **34**, 2333.

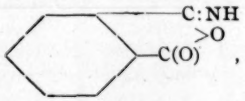
the compound melting at 94° was found to have taken place when the substance stood for some months. When the writer attempted to repeat Mr. Laist's experiment, later, in the University of Berlin, no 94° m. p. 1-phenylacetyl-4-methylurazole could be obtained; the 113°–115° m. p. isomer was always the only product isolated.

All experiments with 1-phenyl-4-methylurazole, or its salts, and acetyl chloride or acetic anhydride, whether in benzene or in ether solution, whether at a low or a high temperature, gave only the 1-phenylacetyl-4-methylurazole, m. p. 113°–115°; the isomer, m. p. 94°, was never isolated in these experiments. It is believed that the 1-phenylacetylurazole, m. p. 175°, and the 1-phenylacetyl-4-methylurazole, m. p. 113°–115°, are probably mixtures of the isomeric 3-oxyacetyl and the 2-acetyl derivatives, melting at the fusing point of the more stable form. A mixture of the labile phenylacetyl-4-methylurazole, m. p. 94°, and the stable form, m. p. 113°–115°, would melt at 113°–115°, because at temperatures close to 94° this labile form would immediately change into the stable form. The melting point of a mixture of these isomers would, then, give no clue as to the amount of each present, but a study of the rate of hydrolysis of these acetyl derivatives by acids or alkalies might offer a method for determining if any specimen is a mixture. The rate of hydrolysis of the 3-oxyacetyl derivative might be different from that for the 2-acetyl isomer, and probably greater than it, and, consequently, the rate of hydrolysis of a mixture would not be uniform as in the case of a single isomer. A study of these and other acyl derivatives will be taken up from this point of view to determine if, in acyl derivatives of tautomeric compounds, there are, in some cases, really 2 isomeric acyl derivatives.

It is evident, then, that unknown differences in condition play very important parts in the formation of these phenylacetylurazoles, and a number of experiments, under varying conditions, were undertaken to secure more light on this subject; the results of this work are now given.

The writer has no disposition to question the facts as pre-

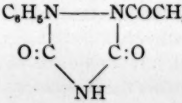
sented by Wheeler and Johnson. It was pointed out that Wheeler and Johnson were working with impure silver phenylurazole, and the conditions employed by these writers could probably never be duplicated again. The case is exactly analogous to that discovered by Remsen[1] and Kuhara; isophthalimide,



was made once and was transformed into phthalimide, but even after many experiments Remsen and Kuhara could never duplicate the conditions necessary to give them again the isophthalimide. The writer has tried very carefully to find the conditions by which pure silver phenylurazole and acetyl chloride could be made to yield Wheeler and Johnson's labile phenyldiacetylurazole.

In general, however, it may be stated that under all conditions pure silver phenylurazole and acetyl chloride gave only pure phenylacetylurazole, m. p. 175°, with sometimes small amounts of phenylurazole and phenyldiacetylurazole and not the products described by Wheeler and Johnson.

1-Phenyl-2-acetylurazole,[2]



.—Ten grams of phenylurazole were boiled 1 hour with 20 grams of acetic anhydride in a flask, under a return condenser. In this reaction phenylurazole was converted into a mixture of 1-phenylacetylurazole and 1-phenyldiacetylurazole. The mass was evaporated with alcohol, one acetyl group of 1-phenyldiacetylurazole was saponified away very much more easily than the other, and 1-phenyl-2-acetylurazole was formed, which is not

[1] This Journal, **3**, 26; **9**, 51; **26**, 454.

[2] Cuneo: Centrabl., 1898, I., 38. Thiele and Schleussner: Ann. Chem. (Liebig), **295**, 171.

readily saponified under these conditions. The mass was digested with 300 cc. of benzene several hours, the benzene was filtered and cooled, and the precipitate of 1-phenylacetylurazole was filtered off. The mass was extracted several times with the same benzene solution and the various crops of 1-phenylacetylurazole were examined; all were apparently alike and melted at 173°–175°. The benzene solution used for the extractions contained some 1-phenyldiacetylurazole, which is very soluble in benzene. The benzene is held somewhat tenaciously by the 1-phenyl-2-acetylurazole, but it evaporates in a desiccator holding paraffin, or in the open air. An attempt was made to free the fresh samples from the benzene by heating the samples in watch-glasses in an air-bath, heated by a gas flame, but it was found that the hot water vapor from the flame saponified the acetyl derivative into acetic acid and phenylurazole.

1-Phenyl-2-acetylurazole is a monobasic acid and in the presence of phenolphthalein titrates sharply against 1 molecule of alkali. It forms a monosilver salt. Cold neutral solutions of the alkali salts are very stable, hardly any hydrolysis of the acetyl group occurring in 12 hours. A sample of the 1-phenylacetylurazole, melting at 173°, titrated against the theoretical amount of 0.1 N potassium hydroxide in the presence of phenolphthalein. Half of this solution was acidified and the 1-phenylacetylurazole precipitated out; when dry, it melted at 171°. The other half of the solution stood over night; the pink color had faded, but it required only 1 drop of 0.1 N potassium hydroxide to restore the pink color. This solution was then acidified and a precipitate of the 1-phenyl-2-acetylurazole was formed, which melted at 171°–172° when dry. When a molecule of potassium hydroxide is added to a solution of an alkali salt of the acetyl derivative and the solution is heated, the acetyl group is saponified off and phenylurazole is formed.

The 1-phenyl-2-acetylurazole is not very readily hydrolyzed when heated in alcohol or water. Nearly 0.45 gram of acetyl derivative, melting at 173°, was dissolved in 25 cc. of alcohol and to this was added 25 cc. of water. This solution was evaporated to dryness on a water-bath in 42 minutes. Crystals

appeared at the edge of the liquid before the end of the operation. When the dish stood in a desiccator 2 days crystals at the edge melted at 163°–165°, showing the presence of considerable phenylurazole formed by hydrolysis, but the main portion in the center of the dish melted at 169°–171°. The substance is readily soluble in hot benzene, cold ether, chloroform, alcohol, but somewhat difficultly soluble in cold benzene, ligroin and water. 1-Phenyldiacetylurazole is difficultly soluble in very cold ether, but easily soluble in benzene, and can, therefore, be separated from the 1-phenyl-2-acetylurazole very easily.

In a former paper it was stated that diazomethane and 1-phenyl-2-acetylurazole yield 1-phenylacetyl-4-methylurazole. This proves that the acetyl group belongs to the 2,3-amide group and not to the 4,5-amide complex. The assumption that the acetyl is at position 2 is only one of convenience. It is believed that all of these samples are mixtures of both forms, in some samples the 2-acetyl derivative occurring in excess and in others the 3-oxyacetyl being the chief constituent, the ratio varying with the conditions attending the formation of the samples. It is probable that the sample methylated by means of diazomethane in Utah by Mr. Laist, and yielding the 1-phenylacetyl-4-methylurazole, m. p. 94°, was chiefly 1-phenyl-3-oxyacetylurazole. The other samples methylated by the writer may have been chiefly 1-phenyl-2-acetylurazole. The differences in climate, barometric pressure, experimental conditions, etc., between the work in the Rocky Mountains and in Berlin may have affected the results. This will be investigated further. Titrations:

1. 0.1895 gram substance required 8.70 cc. 0.0997 N alkali to give a red color (phenolphthalein) and 8.76 cc. to eliminate the acetyl group; calculated, 8.67 cc. for each titration.

2. 0.3126 gram substance required 14.35 cc. 0.0997 N alkali (phenolphthalein); calculated, 14.32 cc.

3. 0.1347 gram substance required 6.14 cc. 0.0997 N alkali (phenolphthalein); calculated, 6.17 cc.

4. 2.1284 grams substance required 98.2 cc. 0.0997 N alkali (phenolphthalein); calculated, 98 cc.

5. 0.2001 gram substance in alcohol required 5.37 cc. 0.1691 N sodium alcoholate in alcohol (phenolphthalein); calculated, 5.40 cc.

6. 5 grams substance dissolved in cold alcohol required 22.80 cc. 1.0 N potassium hydroxide (phenolphthalein); calculated, 22.83 cc.

Analysis:

0.1327 gram substance, m. p. 173°, gave 29.4 cc. N at 32° and 612 mm.

	Calculated for $C_{16}H_8N_2O_3$.	Found.
N	19.22	19.11

On the Action of Acetyl Chloride on Silver Phenylurazole.—Wheeler and Johnson state that by the action of acetyl chloride on silver phenylurazole they obtain no phenylacetylurazole, the normal reaction product, but a labile 1-phenyldiacetylurazole melting at 115°. The writer has never observed the formation of this labile diacetyl derivative, but always obtains, as the chief reaction product, 1-phenylacetyl urazole, m. p. 175°, sometimes accompanied by small amounts of phenylurazole and phenyldiacetylurazole.

I. When 1.5 grams silver phenylurazole was boiled 1 hour with 0.5 gram acetyl chloride, in 20 cc. of benzene, the silver salt seemed to be converted, nearly completely, into silver chloride. The solution was filtered hot and, on cooling, needles of the phenylacetylurazole were formed which melted at 173° alone or mixed with another sample. The silver residue was extracted a second time with benzene, the solutions were combined and evaporated to dryness in a desiccator over paraffin. The residue was crystallized once from benzene and then melted at 172°–173°, whether alone or in mixture. Titration:

0.0675 gram substance required 3.31 cc. 0.0937 N sodium hydroxide for neutralization (phenolphthalein) and then 3.08 cc. to saponify the acetyl group; calculated, 3.28 cc. for each titration. When this solution was acidified pure phenylurazole, melting at 263°, was obtained.

II. When 4 grams of silver phenylurazole were suspended 2 months in absolute ether containing 2 molecular portions of acetyl chloride, the solution was filtered and evaporated. The residue melted at 172°–173°, whether alone or mixed with another sample, m. p. 173°, and at 80°–95°, when mixed with a sample of phenyldiacetylurazole, m. p. 164°. The residue was extracted with hot chloroform, and a small amount of phenylurazole, insoluble in chloroform, melting at 262°, was found. The chloroform solution was evaporated to a small volume and benzene was added; a precipitate of the 1-phenyl-2-acetylurazole was formed, which melted at 176°–177° alone, and at 175° when in admixture with a sample melting at 173°. Titration:

0.1000 gram substance in cold alcohol required 4.90 cc. 0.0937 N sodium hydroxide to neutralize and 4.80 cc. to remove the acetyl group; calculated, 4.87 cc. for each titration. The alkaline solution gave pure phenylurazole, m. p. 262°, when acidified.

III. When 1.5 grams silver phenylurazole were added to 20 cc. benzene containing 0.75 gram of acetyl chloride, the solution became warm. The mixture was agitated for 3 days, and filtered, and the silver chloride residue was washed well twice with benzene. When the silver chloride residue was extracted twice with hot chloroform, and the solution was evaporated, 0.82 gram phenylacetylurazole was obtained, which melted at 174° alone and at 174°–175° when in admixture with a sample melting at 176°. The benzene solutions were united and evaporated in a desiccator over paraffin; a residue of 0.20 gram 1-phenyldiacetylurazole, melting at 160°–162°, alone or in admixture with another sample, was obtained. The silver chloride residue was finally extracted with hot alcohol, filtered, and water was added to the filtrate; a precipitate of 0.10 gram of phenylurazole, melting at 263°, was found. Titration:

0.1000 gram phenylacetylurazole stood 1 hour in alcohol; it then required 5.17 cc. 0.0937 N sodium hydroxide to neutralize (phenolphthalein), and a total of 9.62 cc. to neutralize

and eliminate the acetyl group; calculated, 4.87 cc. and 9.74 cc., respectively.

IV. When 10 grams of silver phenylurazole were boiled 3 hours in ether solution with 5 grams of acetyl chloride, the reaction seemed to be complete. The solution was filtered, the silver residue extracted with ether and filtered again, and the ether solutions were combined and evaporated to dryness in a vacuum. The residue was heated with hot chloroform and filtered from the phenylurazole; the filtrate was evaporated to a small volume and benzene was added, whereupon a precipitate of 2.1 grams of pure phenyl-2-acetylurazole, melting at 170°–173°, was formed. The phenylurazole weighed 0.10 gram.

It is evident, then, that the chief reaction product between silver phenylurazole and acetyl chloride is 1-phenyl-2-acetylurazole, m. p. 173°, and not a labile 1-phenyldiacetylurazole, as described by Wheeler and Johnson. Analysis:

I. 0.1400 gram substance gave 28.6 cc. N at 21° and 631 mm. (corr.).

II. 0.1499 gram substance gave 30 cc. N at 20° and 633 mm. (corr.).

III. 0.1365 gram substance gave 27.5 cc. N at 27.5° and 619 mm. (corr.).

	Calculated for $C_{10}H_9O_3N_3$.	Found.		
		I.	II.	III.
N	19.22	19.33	19.06	19.03

Silver 1-Phenyl-2-acetylurazole.—To 0.5 gram phenyl acetylurazole, m. p. 170°–172°, in 50 cc. of alcohol, was added 22.8 cc. 1.0 N potassium hydroxide and 150 cc. water and the mixture was well cooled. To this solution was added, slowly, a solution of the calculated quantity of silver nitrate, 3.8 grams, the mixture being well agitated with a stirring rod. The precipitate of silver phenylacetylurazole was crystalline and white, and some was left in solution. The precipitate was filtered, washed with water, then with alcohol and afterwards with ether. The ether was removed by suction and the salt was dried in the air. Several samples were made by this method. It is very stable towards light, when freshly pre-

pared. This silver salt seems to contain 1 molecule of water of crystallization, which is lost on standing in the air or in a vacuum desiccator. When the silver salt is heated in an air bath for a short time, at 100°, the acetyl group is saponified by the hot water vapor.

The reaction products of this silver salt and alkyl halides are being studied. Analysis:

I. 0.3081 gram fresh salt gave 0.0956 gram Ag.

II. 0.2755 gram fresh salt gave 0.0847 gram Ag.

III. 0.3040 gram salt dried in desiccator 2 days gave 0.1127 gram Ag.

IV. 0.1441 gram air-dried salt gave 0.0473 gram Ag.

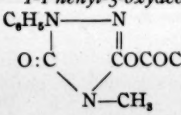
V. 0.1264 gram salt, that had been heated in air-bath at 100° to remove the acetyl group, gave 0.0473 gram Ag.

	Calculated for $C_{10}H_8N_3O_3Ag.H_2O$.	Found. I.	II.
Ag	31.37	31.06	30.71

	Calculated for $C_{10}H_8N_3O_3Ag$.	Found. III.	IV.
Ag	33.13	32.13	32.90

	Calculated for $C_9H_7N_3O_3Ag$.	Found.
Ag	38.03	37.42

1-Phenyl-3-oxyacetyl-4-methylurazole, m. p. 94°,



—A sample of 1-phenylacetylurazole, m. p. 173°, prepared from phenylurazole and acetic anhydride, was treated with an ethereal solution of diazomethane. There was a vigorous evolution of nitrogen and the solid went into solution. The ether was evaporated and the residue was crystallized from a small amount of alcohol; the substance precipitated out in fine needles that melted at 94°–95°. The substance had the same melting point when crystallized from water. When melted and heated to 140°, or when simply kept melted a short time at 95°–100°, and allowed to solidify, it then melted at 113°–115°. When the substance was evapo-

rated with hydrochloric acid several times, or when it was treated with potassium hydroxide, the acetyl group was removed and 1-phenyl-4-methylurazole, melting at 223°, was formed. This shows that the diazomethane methylates the 1-phenylacetylurazole at 4- and not appreciably at 5-. This isomer, m. p. 94°, was never again obtained by this reaction, but the 1-phenyl-2-acetyl-4-methylurazole, m. p. 113°–115°, was always afterwards obtained directly. Analyses:

I. 0.1124 gram phenylacetylmethylurazole gave 22.2 cc. N at 22° and 629 mm. (corr.).

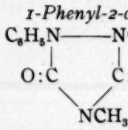
II. 0.1284 gram 1-phenyl-4-methylurazole gave 28.2 cc. N at 17° and 636 mm. (corr.),

III. 0.0993 gram 1-phenyl-4-methylurazole gave 22.8 cc. N at 19°.5 and 631 mm.

	Calculated for $C_{11}H_{11}N_3O_3$.	Found. I.
N	18.06	18.48

	Calculated for $C_9H_9N_3O_3$.	Found. II.	III.
N	22.02	21.30	21.84

1-Phenyl-2-acetyl-4-methylurazole, m. p. 113°–115°,



.—The following is a description of several attempts to prepare the 1-phenylacetyl-4-methylurazole, m. p. 94°, by the action of diazomethane on 1-phenylacetylurazole, and by the acetylation of 1-phenyl-4-methylurazole. It will be noted that the conditions were widely varied, and in some experiments the temperature and pressure were kept as low as possible, to try to prevent a rearrangement during the experiment. All of these experiments gave only the isomer melting, when pure, at 113°–115°.

I. By boiling 5 grams of 1-phenyl-4-methylurazole (m. p. 223°–224°) in 25 grams of acetic anhydride and 5 grams of fused sodium acetate, 2 hours, cooling and adding water to dissolve the sodium acetate, an oily layer was obtained. This was separated and evaporated to dryness with 15 cc.

of absolute alcohol. The residue was crystallized from dilute alcohol and it then melted at 109°–111°.

II. When 25 grams of silver 1-phenyl-4-methylurazole were suspended in ether containing acetyl chloride in slight excess of the calculated amount, and shaken in a bottle 36 hours, the reaction was complete. The silver salt was filtered off and washed with ether, and the combined ether solution was evaporated in a vacuum desiccator, so that the temperature did not rise above 30°. The residue melted at 109°–111°, alone and also when mixed with sample I.

III. A sample of Laist's 1-phenylacetyl-4-methylurazole which, on July 15, 1903, had melted at 94°, fused at 109°–111° without recrystallization on Nov. 8, 1903. Rearrangement had taken place at the ordinary temperature in 4 months.

IV. Part of a sample of 1-phenylacetylurazole, m. p. 173°, which early in 1903 had given 1-phenyl-3-oxyacetyl-4-methylurazole, m. p. 94°, when treated with diazomethane, was, on Nov. 8, 1903, made to react with diazomethane in the same manner. The ether solution was evaporated in a vacuum; the residue melted at 113°–115°. Apparently, then, the sample of 1-phenylacetylurazole had also changed at the ordinary temperature in 4 months.

V. A sample of 2 grams of 1-phenylacetylurazole, m. p. 170°–173°, which was prepared by the action of acetyl chloride on silver phenylurazole, was treated with a slight excess of diazomethane, in ether solution. The solution was divided and one-half was evaporated to dryness in a vacuum desiccator. The residue melted at 110°. The other half of the solution was evaporated over a water-bath, and the sample thus formed also melted at 110°.

VI. Six grams of phenylurazole were boiled 1 hour with 12 grams of acetic anhydride, alcohol was added and the solution was evaporated to dryness. The residue was extracted 2 hours in a Soxhlet extraction apparatus with benzene. The benzene solution gave pure 1-phenylacetylurazole, m. p. 172°–175°, when cooled. Two grams of this acetyl derivative were treated with an ether solution of diazomethane; when the resulting mixture was evaporated to a small volume,

on a water-bath, and dried in a vacuum desiccator, the residue melted at 110°.

VII. A sample of silver phenylurazole was boiled in benzene solution with acetic anhydride, filtered and evaporated to dryness. The residue was treated with an ether solution of diazomethane and the solution evaporated to dryness. The residue melted at 113°.

VIII. In Salt Lake City, Utah, the barometric pressure is about 630 mm. and the boiling point of water about 93°–94°, while in Berlin the barometric pressure is 760–770 mm. In order to see if the lower barometric pressure and the lower boiling points of the liquids were factors concerned in the reaction, phenylurazole was boiled, in benzene solution, with acetic anhydride, under a return condenser, so arranged that the pressure in the apparatus was 70 mm. The reaction took place slowly and the phenylurazole was dissolved. When the benzene solution was cooled, the 1-phenylacetylurazole precipitated out in a very pure state. A sample was treated with diazomethane in ether solution and evaporated to dryness in a vacuum. The residue melted at 113°. Analysis:

0.1329 gram substance, m. p. 113°–115°, gave 21.05 cc. N, collected over 30 per cent potassium hydroxide solution at 27° and 762.9 mm.

0.1737 gram substance, m. p. 113°–115°, gave 26.6 cc. N at 18° and 758 mm. (corr.).

	Calculated for $C_{11}H_{11}N_3O_3$.	Found. I.	II.
N	18.06	17.69	17.64

Conclusions.

1. Experimental work and the application of the mass law show that the relative amounts of the two stable derivatives formed by the reaction of a tautomeric compound, existing in two forms in equilibrium, and another reagent depend upon (1) the relative reactivity of the two tautomeric forms towards the other reagent, (2) the ratio between the amounts of the 2 tautomeric forms when they are in constant equilibrium with each other, and (3) the rapidity of the change of

each of these tautomeric forms into the other as the equilibrium between them is disturbed. In some cases the reaction may be complicated by the rearrangement of one, or each, of the tautomeric derivatives into the other, or some other products.

2. Various phases of the equilibrium condition existing in a solution of a tautomeric acid or base, or the salts, have been studied theoretically, by the application of the mass law, and experimentally. These results are recorded in Sections I. to XVIII., inclusive.

3. The conditions under which normal and abnormal hydrolysis of salts of tautomeric compounds can be determined have been discussed.

4. A large number of derivatives of phenylurazole have been made and studied qualitatively and quantitatively, especially in the light of the theories of tautomeric substances.

JOHNS HOPKINS UNIVERSITY,
Dec. 20, 1906.

SOLUBILITY.

BY EUGENE C. BINGHAM.

HISTORICAL.

As early as in 1790 Lavoisier[1] connected the phenomena of solubility with those of cohesion, but the theory fell into discredit, due principally to the researches of Guy-Lussac.[2] Since that time many different theories of solubility have been proposed, of which only a few can be mentioned here.

The hydrate theory, developed by Pickering[3] and opposed by the advocates of the electrical dissociation theory, sought to explain solubility as due to a combination between the solvent and dissolved substance. This theory was worked out primarily for aqueous solutions.

[1] Ouevres, **1**, 306. *Vide* Alexejew: Wied. Ann., **28**, 327 (1886). Traube: Phil. Mag., (6), **8**, 710 (1904).
[2] Compt. rend., **8**, 1000 (1839).
[3] *Vide* "Solutions," Watts' Dict.

Vaubel[1] based a theory of solubility upon the chemical structure, but for a general theory on this basis great elaboration seems necessary. Carnelly and Thomson[2] concerned themselves with isomers. They showed, quite conclusively, that among isomeric compounds the most fusible are also the most soluble. Nicol,[3] with others,[4] believed that solubility is connected with molecular attraction. Nicol also believed that these attractions are connected with molecular volume.

Although no one of these theories has as yet commended itself sufficiently to be accepted generally by the scientific world, yet it is necessary to bear in mind that each theory accounted for certain facts and is, therefore, probably a partial expression of the truth.

The above workers concerned themselves for the most part with solutions of solids in water. Alexejew[5] was the first to make a systematic study of the simpler case of liquids dissolved in liquids. He found several instances where substances increased in solubility with rise in temperature until, finally, they became infinitely soluble. Guthrie[6] discovered that examples of quite the opposite sort existed where liquids became completely miscible below a certain temperature.

Orme Masson[7] pointed out the important analogy between the temperature of infinite solubility, by him called "the critical solution temperature," and the ordinary critical temperature. Bredig,[8] Noyes,[9] Ewan[10] and Abegg[11] tried to devise formulas of the van der Waals type to apply to these cases.

Rothmund[12] admirably summed up the previous work and extended it by finding several cases of both an upper and a

[1] J. prakt. Chem., (2), **59**, 30 (1899).
[2] J. Chem. Soc., **53**, 782 (1888).
[3] Phil. Mag., (5), **18**, 91.
[4] Kuenen and Robson: *Ibid.*, (6), **6**, 637 (1903).
[5] Wied. Ann., **28**, 305 (1886).
[6] Phil. Mag., (5), **18**, 29, 499 (1884).
[7] Nature, Feb. 12, 1891. Z. physik. Chem., **7**, 500 (1891).
[8] Z. physik. Chem., **4**, 444 (1889).
[9] *Ibid.*, **5**, 53 (1890).
[10] *Ibid.*, **14**, 419 (1894).
[11] *Ibid.*, **15**, 254 (1894).
[12] *Ibid.*, **26**, 433 (1898).

lower critical solution temperature, but no single pair of substances was found showing both of these phenomena. Nevertheless, Rothmund conceived that every pair of substances should, at some temperature, show both an upper and a lower critical solution temperature, making the solubility curve in every case a closed curve. Kuenen and Robson[1] opposed this view on the ground that one of the components might reach its critical temperature before the critical solution temperature was reached.

Hudson[2] found that nicotine and water have an upper critical solution temperature at 210° and a lower critical solution temperature at 60°.

Critical Solution Temperature and the Ordinary Critical Temperature.

The knowledge of a similarity between the critical solution temperature and the ordinary critical temperature is, if real, a most important contribution to our understanding of the phenomenon of solution, for since solubility changes very rapidly near the critical solution temperature, the origin of solubility itself would seem to lie in the explanation of the critical solution temperature. Yet the discussion of this similarity has hardly found its way into the text-books. We believe that this is because: (1) The analogy is not complete, since a liquid in the presence of other liquids may have as many critical solution temperatures as there are liquids, while it has but one ordinary critical temperature. (2) The lower critical solution temperature, in physical appearance much the same as the other, has no apparent analogy to the ordinary critical temperature, nor has an extension of the theory been proposed to account for it, so far as I know. (3) The kinetic theory has not been employed to discover whether there is any relation beyond a mere analogy existing between the phenomena. The want of such a connection has given rise to the belief, as pointed out above, that the ordinary critical temperature might in certain cases intervene and prevent the possibility of a critical solution temperature.

[1] Phil. Mag., (6), **6**, 637 (1903).
[2] Z. physik. Chem., **47**, 113 (1904).

If we keep before us the fact that the liquid and gaseous states of matter are continuous I think that it may be shown that this apprehension is unfounded and, moreover, that an interesting connection appears between the critical solution temperature and the ordinary critical temperature. We may take ethane and water as an example. Ethane reaches its critical temperature before complete solubility takes place, but, since all gases are miscible, at some temperature below the critical temperature of water, ethane must be completely soluble in water, if the pressure is sufficiently great. The temperature of complete solubility must be regarded as the critical solution temperature. The figure

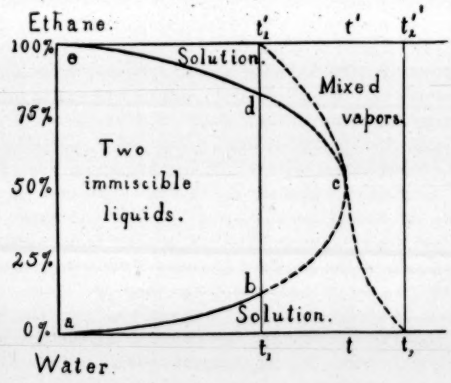


Fig. I.

will make this point clearer. Ordinates represent percentages of ethane, and abscissas temperatures. We assume that the pressure is equal to the vapor pressure of the mixture under consideration, or, what amounts to practically the same thing, that the experiments are made at a constant volume. If t_1 and t_2 represent the critical temperatures of ethane and water, respectively, *ab* is the solubility curve of ethane in

water, *de* that of water in ethane; *bc* represents the increasing solubility of ethane gas in water, as the temperature rises, and *cd* represents, finally, the limit of solubility of water in ethane gas; *c* is, then, the critical solution point and *t* is the critical solution temperature, situated between t_1 and t_2.

Two liquid phases exist within the area *abcde*. Of the remainder of the figure, the part to the right of the curve, ($t' ct_2$) represents mixtures of ethane and water vapor which cannot be liquified by pressure. The part to the left of this curve represents a single liquid phase. The curve ($t' ct_2$) represents, therefore, the points at which the liquid solutions are in equilibrium with the vapor mixtures. Stated differently, it represents the critical temperatures of aqueous ethane solutions, or the amounts by which the critical temperature of water is lowered by the addition of successive amounts of ethane. We may call this a critical temperature curve since the critical temperature of ethane and water form the two limiting values and each intermediate point represents the critical temperature of a solution of definite concentration of ethane in water or of water in ethane.

If we consider ethane and water to be a limiting case, for the purpose of illustration, we see that the solubility curve will touch the critical temperature curve at the point *c*, though it cannot cross that curve. Whether or not there might be 2 or more points in common between these curves we do not need to consider here. As a point on the critical temperature curve this point defines a temperature, for the given concentration, above which no pressure will cause the mixture to separate into 2 phases of liquid and vapor. As a point on the solubility curve, it defines a temperature, for the given concentration, above which no pressure will cause the mixture to separate into 2 liquid phases. There is thus the most intimate connection beween the critical solution temperature and the critical temperature of a mixture. There is, in fact, a certain analogy between the 2 curves throughout their whole course.

Returning to the figure, we see that inside of the area $a\ b\ t_1$ we have aqueous solutions of liquid ethane. The area $b\ c\ t_2 t_1$

defines the possibilities of liquid aqueous solutions of ethane gas. In the area $d\,e\,t'_1$, we have solutions of water in liquid ethane. $D\,c\,t'^1$ gives the limits within which we may have water dissolved in ethane gas, the solution being liquid under sufficient pressure, due to the elevation of the critical temperature of the ethane by the water. *Heretofore the solution of a gas (or vapor) in another gas (or vapor), of a gas (or vapor) in a liquid, and of a liquid in a liquid have been regarded as quite distinct. We note, however, from the above considerations that no sharp line of demarcation can be drawn between them.*

Significance of the Critical Solution Temperature.

To make the above connection between the critical solution temperature and the ordinary critical temperature somewhat clearer, let us turn to the kinetic theory for the origin of each.

When a liquid is heated in a closed space, certain molecules near the surface have kinetic energy sufficient to overcome the forces of cohesion in the liquid and become a part of the superincumbent vapor. As the liquid is heated, it expands, in general, due to the increased velocity of the molecules. Thus the kinetic energy of the molecules causes them to behave as though they actually repelled each other with a force increasing with the temperature, so more and more particles pass off as the temperature is raised. Moreover, the particles of the vapor itself finally become so closely crowded that they exert a mutual attraction for each other and also for the liquid, hence more liquid vaporizes than we should expect if the vapor obeyed the gas laws. At length the forces of attraction in the liquid for a particle at its surface become just equal to the repellant forces, due to the kinetic energy of the molecules. Thus a liquid at this temperature possesses just sufficient energy to expand indefinitely—we have reached the gaseous state. The surface separating the liquid and vapor necessarily vanishes, all the properties of liquid and gas are identical at this, the critical temperature.

The particles within the vessel, striking the walls, give rise to a pressure, in this case the critical pressure. This force we

believe to be a measure of what we have spoken of as the repellant forces due to the kinetic energy of the molecules, but since these repellant forces are just equal to the attractive forces between the molecules at the critical temperature, the critical pressure is an exact measure of the attractive forces between the molecules themselves at the critical temperature.

In case there are gases present in addition to the liquid in question and its own vapor, the case is more complicated. The gas will have a certain attractive force for the molecules of vapor and also for the particles at the surface of the liquid. Dalton's law states that these effects are negligible at ordinary temperatures, but they may become very important as we approach the critical temperature. The critical temperature is known to be considerably altered by small amounts of foreign substances. The gas may also be dissolved in the liquid to some extent affecting the magnitude of the attractive forces in the liquid.

Now let us suppose that the space above our liquid is filled with another liquid which is immiscible with the first, instead of a foreign gas. The first liquid will send particles into the second exactly analogous to the process of vaporization described above, where a foreign gas is present. These particles wander about in their respective solvents quite as independent of each other as do the particles of a gas, so long as the solutions are not concentrated. Thus, if we measure effects in which these particles alone are concerned, we find them obeying the laws of gases, the most noticeable difference between the two being the slower motion in liquid diffusion than in gaseous diffusion, due to the friction caused by the solvent medium.

As the temperature is raised the liquids, in general, expand, and since the attractive forces become lessened thereby, more particles of each are enabled to pass into solution in the other liquid. The dissolved particles finally become so crowded together that they are no longer independent of each other, *i. e.*, their osmotic pressures no longer obey the gas laws. When the forces tending to bring the liquids into solution are

just equal to the sum of the *cohesive* forces between the particles of each liquid, the surface separating the two liquids vanishes, and all parts of the mixture become identical as soon as the system has reached a steady state. This is the critical solution temperature.

Necessary Condition for an Upper Critical Solution Temperature.

The statement of the necessary condition for a critical solution temperature set forth in the preceding paragraph may be made more reasonable and formulated by the following considerations:

Suppose O, in Fig. II., to be a point on the surface $m\,n$ between 2 liquids A and B, which are saturated with respect to each other at a given constant temperature. We may

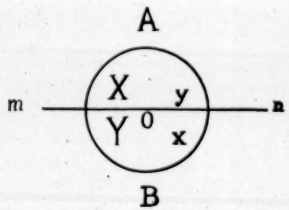


Fig. II.

imagine a sphere described about O, of which the circle is a cross-section, of such size that the molecular forces acting on a molecule at O are negligible outside of the sphere. Let X represent the number of molecules of A in the upper hemisphere and x those in the lower hemisphere dissolved in B. Let Y and y represent the numbers of molecules of B in the lower and upper hemispheres, respectively. In either hemisphere the distribution must be uniform when the system has reached a steady state, otherwise diffusion would take place between the different parts, and the solution could not have been saturated.

The attraction of a particle of A at the point O by the X particles of A, may be represented by some function of X, as $\phi(X)$, in which the coefficient of attraction between 2 molecules of A and the rate of variation of this force with the distance must appear, the components of all of the individual forces at right angles to $m\,n$ being summated for the whole hemisphere. This resultant force will evidently be a force acting upwards at the point O at right angles to $m\,n$. Since adhesion is as universal a property of matter as is cohesion, the y particles of B dissolved in A must exert an attraction for the particle of A at the point O. The coefficient of attraction beween a particle of A and a particle of B will now appear. Let this force be represented by $\xi(y)$. The attraction of the Y particles of B in the lower hemisphere for the particle of A at O will be entirely similar to $\xi(y)$ and will be some multiple of it, $\xi(Y)$ depending merely upon their ratios. We have assumed here that the rate of variation of the attraction with the distance is independent of the number of particles. Similarly the attraction of the x particles of A will be represented by $\phi(x)$. We have, then, the total force acting upwards on a particle of A at O due to the upper hemisphere equal to

$$\phi(X) + \xi(y) \quad \ldots \ldots \ldots \quad (1),$$

and the total force acting upwards due to the lower hemisphere, equal to

$$-[\xi(Y) + \phi(x)] \quad \ldots \ldots \ldots \quad (2).$$

In like manner, if we consider the forces acting upwards on a particle of B at O, we have

$$-[\psi(Y) + \xi(x)] \quad \ldots \ldots \ldots \quad (1a),$$

due to the lower hemisphere, and

$$\xi(X) + \psi(y) \quad \ldots \ldots \ldots \quad (2a),$$

due to the upper hemisphere.

The resultant upward force on a particle of A at O, due to all of the particles in both hemispheres, is

$$\phi(X-x)-\xi(Y-y) \quad \ldots\ldots\ldots\ldots (3),$$

and the resultant upward force on a particle of B at O is, similarly,

$$-[\psi(Y-y)-\xi(X-x)] \quad \ldots\ldots\ldots\ldots (4).$$

Now these two expressions, (3) and (4), may each be either greater or less than zero. If

$$\phi(X-x)+\xi(Y-y)>O,$$

work will need to be done against this force by every particle of A that goes into solution in B, and this will tend to prevent the 2 liquids from mixing completely. On the contrary, if the total upward force on a particle of A is less than zero, *i. e.*, if the force acts downwards, work will be gained by the particle in moving into the lower hemisphere; but the process of going into solution in B dilutes the liquid B, so that its particles are moved away from each other and towards the liquid A. This may, or may not, call for the expenditure of work, according as

$$-[\psi(Y-y)-\xi(X-x)]$$

is greater or less than zero, respectively. Any change in the total volumes of the liquids has been here neglected. If, then,

$$\phi(X-x)-\xi(Y-y)<-[\psi(Y-y)-\xi(X-x)],$$

or

$$\phi(X-x)+\psi(Y-y)<\xi(X-x)+\xi(Y-y) \quad \ldots (5),$$

we have the condition for complete miscibility, for work will on the whole, be gained by the process of reciprocal solution of A in B and of B in A. The forces in the left hand member oppose, while those in the right hand member aid the process of solution.

If

$$\phi(X-x)+\psi(Y-y)=\xi(X-x)+\xi(Y-y) \quad \ldots (6),$$

no work will be done in moving any particle of the mixture from one part to another, and we have the condition for the

critical solution temperature. We know from the results of experiment that the above equation must hold at the critical solution temperature, since at this temperature the differences of concentration become zero and, hence, the above equation becomes identically equal to zero.

In case

$$\phi(X-x)+\psi(Y-y)>\xi(X-x)+\xi(Y-y) \ldots (7),$$

work will, on the whole, need to be done upon the particles of A and B as they go into solution. Hence, only those particles which are especially favorably situated will be able to pass the bounding surface between the two liquids, and of those that have passed into solution some will continually be drawn out of solution as they come into the range of the attractive forces at the bounding surface. So under these conditions, the amount of each liquid in each solution in the other at any time has a definite limiting value depending upon the magnitude of the difference between the 2 members of equation (7), as well as upon the temperature; in other words, the liquids are immiscible.

Partial and Complete Solubility.

Using the above conception of the criteria of miscibility, I may point out a distinction between partial and complete solubility, which, as far as I know, has not been made up to this time.

If a little aniline be added to a large flask of water, the aniline goes to the bottom in drops which gradually diminish in size and finally disappear. Sharply to be distinguished from this case is that of acetic acid and water, brought together in a similar manner. The acetic acid mixes with the water at once, the meniscus between the two in no case remains sharply defined—the two liquids are completely miscible. There is a condition of unstable equilibrium established whenever acetic acid and water are brought together until they are perfectly mixed; and the mixture must take place as rapidly as diffusion will allow, down to the temperature where the solid phase makes its appearance.

In the case of aniline and water, a sharp meniscus is present, the aniline falls through the water in globules; a few of those particles which are near the surface of separation may have sufficient kinetic energy to do the work necessary to go into solution in the water. Thus, the aniline gradually all passes into solution because, under the above conditions, very few of the aniline molecules come back again into the range of attraction of the remaining portion after having once escaped, but while the aniline remains partly undissolved, each drop is surrounded by a layer of nearly saturated solution of aniline in water and the conditions for immiscibility hold. The same considerations apply when small amounts of water are added to a large volume of aniline.

As we perform the experiment of adding aniline to water at higher and higher temperatures, the above distinction becomes less and less clearly marked, and finally disappears at the critical solution temperature, 165°. Above this temperature the case is similar to that of acetic acid and water. Thus, *below the critical solution temperature we have only mutual partial solubilities, but above this temperature there is complete miscibility.* We may, therefore, speak of mixtures at temperatures above the critical solution temperature and of solutions below that temperature. *The solvent may then be regarded as that pure substance toward which the solubility curve recedes with falling temperature.*

The Lower Critical Solution Temperature.

The usual course of liquid substances seems to be from immiscibility to complete miscibility as the temperature is raised. This results from the increase in the kinetic energy of the particles, as already pointed out. It is possible, however, that certain liquids may have a chemical attraction for each other in addition to the ordinary physical attraction. This force would decrease with rising temperature, so that we may distinguish 4 typical cases:

1. In the ordinary simplest case, represented by aniline and water, the mutual solubilities gradually increase up to the critical solution temperature.

2. Should a chemical or other attraction come in, which, although not strong enough to reduce the work done by mutual solution to zero, is yet able to affect the solubility curves, possibly causing the solubility to decrease as the temperature is raised over a certain range. This case is typified by mixtures of secondary butyl alcohol and water, as observed by Alexejew,[1] where there is a minimum and maximum in the upper and lower branches, respectively, of the solubility curve.

3. If, however, the chemical attraction is greater than the above value, we have the condition of miscibility, and we have a critical solution temperature. Thus we have the possibility of 2 critical solution temperatures for the same pair of substances, an upper and usual critical solution temperature, and a lower, *false* critical solution temperature, due to the introduction of a new attraction, perhaps chemical in its nature, between the components. If it is, indeed, caused by a chemical attraction, we may properly call this a false critical solution temperature, for we then have a third substance formed by the union of the other 2 and we have, therefore, entirely new conditions of mixture.

Only mixtures of nicotine and water have thus far yielded both an upper and a lower critical solution temperature. Hudson,[2] who studied this case, believed that the phenomena were to be explained by a weak chemical combination, but several cases are known which probably fall into this class. Triethylamine and water[3] is the best instance. They are miscible up to 18°.3, where they become quite immiscible. Somewhat beyond this temperature the mutual solubilities seem to increase with the temperature, as in the usual case. Diethylamine and water show the same phenomena, but the false critical solution temperature is higher than in the former case. The other members of the series, ethylamine and ammonia, have not been found to be immiscible with water at any temperature. It is evident that each of these pairs

[1] *Loc. cit.*
[2] *Loc. cit.*
[3] Guthrie: *Loc cit.* Rothmund: *Loc. cit.*

of liquids may exhibit chemical attraction. It would appear, then, that this attraction grows less and less as we descend the series, which is in accord with what we know of other properties. Another pair of liquids which Rothmund[1] found to have a lower critical solution temperature is that of collidine and water. Here, again, we have the possibility of combination. Pyridine and water have not been found to be immiscible at any temperature, and we should expect the tendency toward combination to be more strongly shown by the latter. More recently, Kuenen[2] and Buchner[3] have found several cases of a lower critical solution temperature, where water is not one of the components. Of these *o*-nitrophenol and carbon dioxide, found by Büchner to be immiscible above 39°.5, is obviously in harmony with the preceding explanation.

4. Since the solubility curve in the above case passes through 2 critical solution temperatures, we have there a closed curve of a more or less elliptical nature. If, however, this closed area becomes reduced to a mere point, we have a fourth case, which seems to be typified by ammonia and water, pyridine and water, and alcohol and water, no critical solution temperature being observed at any temperature.

The forces which come into play in causing crystallization may also prevent us from finding a critical solution temperature.

Measure of Molecular Attraction.

The law of Avogadro holds, so far as we know, for all similar particles which are far enough apart, so that the time during which the particles are in the range of each other's attraction is negligible in comparison with the time that they are outside of this range. It seems to make no difference whether other dissimilar particles, gases, liquids, or even solids are present or not. As we bring the particles nearer, however, they attract each other more and more. This attraction between the particles is proved in many ways, such as by the

[1] *Loc. cit.*
[2] *Loc. cit.*
[3] Z. physik. Chem., **54**, 665 (1906).

Joule-Thomson effect in imperfect gases and by the cohesion of liquids. Thus, it occurred to me that the deviations from Avogadro's law might give a measure of the attractive forces between the particles of different substances at any given temperature. This would signify that the attractive forces are inversely proportional to the molecular volumes, but this assumption is open to the objection that the real volume of the molecules themselves may also have an effect upon the apparent molecular volume, *i. e.*, the volume effectively occupied by the molecules. It has been customary, because convenient, to consider molecular volumes from the merely spacial standpoint rather than from the point of view that the "effective molecular volume" is a result of the equilibrium of attractive and repellant forces. The known facts in regard to the additivity of atomic volumes would seem to be explained equally well on either basis, but regarding molecular-volumes as a measure of the attractive forces brings us face to face with the question, how far does the real volume of the molecule affect the apparent, or ordinary molecular volume.

In order to answer this question, I have sought for other methods of measuring molecular attraction. It has been already shown (p. 97) that the critical pressure is a measure of the attractive forces between the molecules at the critical temperature and I hope to give the mathematical evidence in favor of this view at a later time. If the critical pressure is a measure of molecular attraction, and if molecular volume is assumed to be inversely proportional to molecular attraction, then the deviation of their product for different substances from a constant value may be relied upon as a test of the accuracy of my assumption.

Strictly, we should use the molecular volumes of substances at the critical temperature only; but few determinations of critical densities are known and these are subject to some uncertainty, so that the molecular volumes of substances at their boiling points, which are approximately corresponding temperatures, would seem to give a more satisfactory basis for comparison.

The following table gives the results obtained by using the molecular volumes at both of these temperatures for a few substances of very diverse character. I have also used the molecular volumes at the ordinary temperature, 20°, because this is the temperature at which we most wish to know the molecular attractions and because the molecular volumes of our substances vary rather slowly with the temperature; hence, we may expect the values of the product of the molecular-volume and the critical pressure to differ in no marked degree from those at the boiling point, for ordinary substances. M is the molecular weight of the substance; ρ, ρ_b, ρ_c, the density at ordinary temperature, at the boiling point, and at the critical temperature, respectively. The critical pressure is represented by π. Columns VIII., IX. and X. contain the respective molecular volumes; and columns XI., XII. and XIII. the products of molecular volume and critical pressure. When we consider that the values for the critical pressure given for one and the same substance differ by as much as 20 per cent and that the substances chosen have been selected merely with a view of getting well known representatives of many different classes of compounds, both associated and unassociated, the agreement is surprising. It is everywhere within the possible limits of experimental error, which are, of course, large.

Since the values of the b of van der Waal's equation are proportional to the volumes of the particles, it is interesting to compare this constant with the molecular volumes. The products of the critical pressure and the values of b are given in column XV. of Table I. The agreement is not very good, although, perhaps, within the limits allowed by the uncertainties of π and b, but the point which I wish to make is that the substances which give great deviation from the mean value of the constant $\pi\frac{M}{\rho}$ also give, in general, large deviations for the values of πb and in the same direction. We should expect precisely this result if the values of π were, in certain cases, considerably in error.

Table I.

I. Substance.	II. Formula.	III. M.	IV.		ρ.	V. ρb.	VI. ρc.	VII. π.	VIII. $\frac{M}{\rho}$.	IX. $\frac{M}{\rho b}$.	X. $\frac{M}{\rho c}$.	XI. $\pi\frac{M}{\rho}$.	XII. $\pi\frac{M}{\rho b}$.	XIII. $\pi\frac{M}{\rho c}$.	XIV. b.	XV. πb.	XVI. a^2 mm. at 20°.
Water	H_2O	18.0	20/20	1.00	0.9587	0.429	197.0	18.0	18.8	42.0	3550	3700	8300	0.00150	0.295	14.82
Methyl alcohol	CH_4O	32.0	20/4	0.7953	0.7483	0.273	79.0	40.2	42.8	117.6	3180	3380	9300	0.00300	0.237	5.94
Acetic acid	$C_2H_4O_2$	60.0	20/	1.0514	0.9325	0.351	57.0	57.0	64.3	171.1	3250	3670	9800	0.00474	0.268	5.02
Ethyl alcohol	C_2H_6O	46.0	15/15	0.7942	0.7339	0.2755	62.8	57.9	62.7	167.0	3640	3940	10400	0.00377	0.237	5.89
Carbon disulphide	CS_2	76.1	0/4	1.2922	1.2224	....	75.0	58.9	62.2	....	4420	4660	....	0.0033	0.247	5.38
Acetone	C_3H_6O	58.0	13.9/0	0.7994	0.7537	....	56.0	72.5	70.8	....	4060	3960	....	0.00444	0.246	5.87
Chloroform	$CHCl_3$	119.4	11.8/4	1.5039	1.3954	0.370	54.9	79.4	85.6	323.0	4360	4700	17700	0.00445	0.244	3.75
Benzene	C_6H_6	78.0	14/4	0.8839	0.812	0.304	47.9	88.2	96.0	256.1	4220	4610	12300	0.0048	0.230	6.73
Aniline	C_6H_7N	93.1	4.6/4	1.0276	0.8527	....	52.0	90.6	109.2	....	4710	5860	....	0.00611	0.317	8.73
Carbon tetrachloride	CCl_4	153.8	0/4	1.5947	1.4658	0.5576	45.0	97.1	105.0	276.0	4370	4720	11400	0.00434	0.195	3.29
Phenyl chloride	C_6H_5Cl	112.5	21/0	1.1058	0.981	0.3654	44.6	101.7	114.6	307.9	4540	5110	13700	0.00650	0.290	3.77
Ether	$C_4H_{10}O$	74.1	15/4	0.7191	0.6956	0.260	37.8	103.0	106.5	282.0	3890	4260	10200	0.00563	0.202	4.72
Stannic chloride	$SnCl_4$	260.8	....	2.28	1.978	0.7419	36.9	114.4	131.9	351.5	4220	4890	13000	0.00733	0.271	....
Hexane	C_6H_{14}	86.1	17/0	0.663	0.6199	0.2344	30.0	129.9	139.0	367.3	3900	4170	11000	0.0078	0.234	5.41
Triethylamine	$C_6H_{15}N$	102.2	15/0	0.735	0.6621	....	30.0	137.6	152.8	....	4130	4580	....	0.00818	0.245	....
Decane	$C_{10}H_{22}$	142.2	15/0	0.7342	0.6475	....	21.0	193.6	229.4	....	4070	4820	....	0.0130	0.273	....

It may properly be asked whether cohesion can be used to measure molecular attraction, for it is certainly true that cohesion is a result of the attractive forces between the molecules, but that cohesion is not a direct and absolute measure of these forces seems equally certain, because cohesion becomes zero at the boiling point, while molecular attraction becomes zero only in the ideal gas. If, however, the critical pressure is a measure of the molecular attraction at the critical temperature and pressure, the values of cohesion at that pressure for lower temperatures might be regarded as increments of molecular attraction. Cohesion is ordinarily measured under atmospheric pressure and at near the ordinary temperature, so it is not to be expected that the values obtained as increments will be proportional to the molecular attraction. The values for the surface-tension of the substances in Table I. are given in column XVI.

Table II. gives the values of the constant $\pi\frac{M}{\rho}$ for all substances for which sufficient data could be found in the literature. For reasons enumerated before, I have used the values of the density at the ordinary temperature. The agreement is of the same order already observed. To show that much of the deviation from the mean value may be explained by the personal equations of the different investigators and the errors of measurement, I have starred the values obtained by a single investigator, Professor Young, to whom we are indebted for many careful determinations of the critical pressure. Seventeen of his 20 values give an average deviation from the mean value of 3920 of only 3.7 per cent. The value for phenyl iodide is over 40 per cent too great, but it is to be noted that the figures for the critical pressure of this substance were calculated, and not obtained by direct observation. These values are grouped together in Table III.

There seems to be a tendency for the product of the molecular volume and critical pressure to increase with the molecular volume, but the effect is hardly recognizable. For our present purposes, we shall, then, regard the product as a constant and the molecular volume as a measure of molecular attrac-

Table II.

Substance.	Formula.	M.	*t.*	ρ.	$\frac{M}{\rho}$	π.	$\pi\frac{M}{\rho}$.	*b.*	πb.
Mercury	Hg	200.0	20/4	13.546	14.8	....	....	.....	.....
Phosphorus	P	31.0	44.2/	1.7555	17.6	....	...	.....	.....
Sulphur	S	32.0	113/	1.811	17.7	...	....	.....	.....
Water	H_2O	18.0	20/20	1.00	18.0	197.0	3500	0.00150	0.295
Sodium	Na	23.0	97.6/0	0.9287	24.8	....	....	.....	.....
Bromine	Br	80.0	20/	3.120	25.7	....	....	.....	.....
Ammonia	NH_3	17.0	20/	0.6089	28.0	114.0	3200	0.00162	0.285
Hydrogen sulphide	H_2S	34.1	18.5/	0.91	37.4	90.0	3370	0.00189	0.170
Formic acid	CH_2O_2	46.0	20/4	1.2213	37.7	....	....	.....	.....
Silver nitrate	$AgNO_3$	260.8	...	4.33	39.2	....	....	.....	.....
Methyl alcohol	CH_4O	32.0	20/	0.7953	40.2	79.0	3180	0.00300	0.237
Hydrochloric acid	HCl	36.4	15.8/	0.835	43.6	86.0	3750	0.00173	0.149
Sulphur dioxide	SO_2	64.1	20.6/	1.3769	46.5	78.9	3670	0.00249	0.196
Acetonitrile	C_2H_3N	41.0	16/	0.8191	50.0	47.7	2380	.....	.....
Nitrous oxide	N_2O	44.0	20/	0.758	52.6	75.0	3940	0.00189	0.141
Carbon dioxide	CO_2	44.0	20/	0.8267	53.2	73.0	3800	0.00190	0.138
Sulphuric acid	H_2SO_4	98.0	15/	1.838	53.3	....	....	.....	.....
Methyl chloride	CH_3Cl	50.5	17.9/	0.9197	54.9	73.0	4010	0.00260	0.190
Acetic aldehyde	C_2H_4O	55.6	16/	0.7876	55.6	....	....	.....	.....
Acetic acid	$C_2H_4O_2$	60.0	20/	1.0514	57.0	57.0	3250	0.00474	0.268
Ethyl alcohol	C_2H_6O	46.0	15/15	0.7942	57.9	62.8	3640	0.00377	0.237
Carbon disulphide	CS_2	76.1	0/4	1.2922	58.9	75.0	4400	0.0033	0.247
Cyanogen	C_2N_2	52.1	17.2/	0.866	60.2	61.7	3710	0.00290	0.179
Methyl formate	$C_2H_4O_2$	60.1	15/	0.9797	61.3	61.6*	3770	0.0360	0.222

Table II. (Continued).

Substance.	Formula.	M.	*t.*	*ρ.*	$\frac{M}{\rho}$.	π.	$\pi\frac{M}{\rho}$.	*b.*	πb.
Ethylamine	C_2H_7N	45.1	8/1	0.6964	65.0	66.0	4290	0.00312	0.206
Propionitrile	C_3H_5N	55.1	4/	0.7998	68.8	41.3	2800	.....	.....
Ethyl chloride	C_2H_5Cl	64.5	15/	0.9230	69.9	53.0	3700	0.00391	0.207
Acetone	C_3H_6O	58.0	13.9/	0.7994	72.5	56.0	4060	0.00444	0.246
Propyl alcohol	C_3H_8O	60.1	20/	0.8044	74.7	50.2*	3750	0.00490	0.246
Isopropyl alcohol	C_3H_8O	60.1	20/	0.7887	76.2	53.0	4050	0.00438	0.233
Glycerol	$C_3H_8O_3$	92.1	13/	1.2691	78.0	....	....	.....	.....
Ethylene chloride	$C_2H_4Cl_2$	98.9	20/	1.2521	79.0	53.0	4190	0.00485	0.257
Pyridine	C_5H_5N	79.1	15/	0.9855	79.2	....	....	.....	.....
Chloroform	$CHCl_3$	119.4	11.8/4	1.5039	79.4	54.9	4360	0.00445	0.244
Methylene iodide	CH_2I_2	264.9	15/	3.2853	80.6	....	....	.....	.....
Ethyl formate	$C_3H_6O_2$	74.1	20/	0.9064	81.7	46.8*	3830	0.00497	0.233
Methyl acetate	$C_3H_6O_2$	74.1	20/	0.9039	82.0	47.5*	3890	0.00501	0.238
Propylamine	C_3H_9N	59.1	20/	0.7186	82.2	50.0	4110	0.00450	0.225
Ethylidene chloride	$C_2H_4Cl_2$	98.9	20/	1.1743	84.2	52.0	4070	0.0046	0.239
Methyl ethyl ether	C_3H_8O	60.1	10.8/	0.7127	84.3	46.3	3910	0.00436	0.202
Ethylene bromide	C_2H_4Br	188.0	20/	2.1785	86.3	70.6	6090	.....	.....
Trimethylamine	C_3H_9N	59.1	0/	0.673	87.8	41.0	3600	0.00484	0.198
Propyl chloride	C_3H_7Cl	78.5	20/	0.8892	88.2	49.0	4320	0.00461	0.226
Benzene	C_6H_6	78.0	14/4	0.8839	88.2	47.9*	4220	0.0048	0.230
Phenol	C_6H_6O	94.1	50/	0.1466	89.9	....	....	.....	.....
Aniline	C_6H_7N	93.1	11.6/4	1.0276	90.6	52.0	4710	0.00611	0.317
Isobutyl alcohol	$C_4H_{10}O$	74.1	20/	0.8025	92.3	48.3	4460	0.00510	0.246
Isobutyric acid	$C_4H_8O_2$	88.1	20/4	0.9515	92.6	....	....	.....	.....

Table II. (Continued).

Substance.	Formula.	M.	*t.*	*ρ.*	$\frac{M}{\rho}$	π.	$\pi\frac{M}{\rho}$.	*b.*	πb.
Resorcinol	$C_6H_6O_2$	110.0	110/	1.1824	93.1	....	....	.....	.....
Phenyl fluoride	C_6H_5F	96.1	20/	1.024	93.8	44.6*	4240	0.00575	0.256
Piperidene	$C_5H_{11}N$	85.1	4/	0.8814	96.5	45.9	4430	.....	.....
Carbon tertrachloride	CCl_4	153.8	0/4	1.5947	97.1	45.0	4370	0.00434	0.195
Propyl formate	$C_4H_8O_2$	88.1	14/	0.9026	97.6	40.6*	4170	0.00615	0.246
Ethyl acetate	$C_4H_8O_2$	88.1	20/	0.9007	97.8	38.0*	3720	0.00312	0.206
Methyl propionate	$C_4H_8O_2$	88.1	14/	0.8954	98.4	39.5*	3890	0.00414	0.242
Thiophen	C_4H_4S	84.1	20/	1.0651	99.4	47.7	4740	0.00567	0.260
Benzoic aldehyde	C_7H_6O	100.0	15/	0.987	101.4	....	....	.....	.....
Phenyl chloride	C_6H_5Cl	112.5	21/	1.1058	101.7	44.6	4540	0.00650	0.290
Benzoic acid	$C_7H_6O_2$	122.0	121.4/	1.0838	102.6	....	....	.....	.....
Benzonitrile	C_7H_5N	103.1	18/	1.0052	102.6	41.6	4270	0.00770	0.320
Ethyl ether	$C_4H_{10}O$	73.1	15/4	0.7191	103.0	37.8	3890	0.00563	0.202
Diethylamine	$C_4H_{11}N$	73.1	20/	0.7055	103.6	39.0	4040	0.00572	0.223
Nitrobenzene	$C_6H_5NO_2$	123.1	14.4/	1.1866	103.8	....	....	.....	.....
m-Cresol	C_7H_8O	108.1	19/	1.033	104.7	45.0	4710	0.00717	0.322
Phenyl bromide	C_6H_5Br	157.0	20/	1.4914	105.3	44.6 calc.	4700	0.00688	0.307
Isoamyl alcohol	$C_5H_{12}O$	88.1	18.7/	0.8113	105.5	....	....	.....	.....
Toluene	C_7H_8	92.1	13.5/4	0.8708	105.7	41.6	4400	0.00653	0.272
m-Toluidine	C_7H_9N	107.1	25/	0.998	107.3	....	....	.....	.....
Valeric acid	$C_5H_{10}O_2$	102.1	20/	0.9415	108.4	....	....	.....	.....
Anisol	C_7H_8O	108.1	21.8/	0.9878	109.4	41.2	4500	0.00712	0.293
Methyl isobutyrate	$C_5H_{10}O_2$	102.1	0/	0.9056	110.2	33.9*	3740	0.00730	0.247

Table II. (Continued).

Substance.	Formula.	M.	*t*.	ρ.	$\frac{M}{\rho}$.	π.	$\pi\frac{M}{\rho}$.	*b*.	πb.
Naphthalene	$C_{10}H_8$	128.1	18/	1.153	111.1	39.2	4350	0.00865	0.338
Methylbutyrate	$C_5H_{10}O_2$	102.1	20/	0.8962	111.4	34.2*	3810	0.00730	0.249
Propyl acetate	$C_5H_{10}O_2$	102.1	20/	0.8856	112.7	33.2*	3740	0.00758	0.252
Germanium tetrachloride	$GeCl_4$	214.3	18/	1.887	113.6	38.0	4300	0.00663	0.255
Pentane	C_5H_{12}	72.1	17/	0.6323	114.0	33.0	3760	0.00652	0.212
Stannic chloride	$SnCl_4$	260.8	....	2.28	114.4	36.9*	4220	0.00733	0.271
Isopentane	C_5H_{12}	72.1	18/	0.628	114.8	33.0*	3790	0.00641	0.233
Ethyl propionate	$C_5H_{10}O_2$	102.1	19/	0.8900	114.8	33.2*	3810	0.00754	0.250
Hexane	C_6H_{12}	84.1	20/4	0.7287	115.4	39.8*	4590	0.00636	0.254
Acetophenone	C_8H_8O	120.0	15/	1.032	116.3	....	....	.....	.....
Isobutylformate	$C_5H_{10}O_2$	102.1	14/	0.8650	118.0	38.3	4520	0.00659	0.252
Capronitrile	$C_6H_{11}N$	97.1	20/	0.8061	120.5	32.1	3870	0.00886	0.284
Ethylbenzene	C_8H_{10}	106.1	20/	0.8673	122.3	38.0	4650	0.00744	0.283
m-Xylene	C_8H_{10}	106.1	20/	0.8655	122.6	35.8	4390	0.00791	0.272
o-Xylene	C_8H_{10}	106.1	18/	0.8632	122.9	36.9	4530	0.00784	0.289
p-Xylene	C_8H_{10}	106.1	19.5/	0.8621	123.1	35.0	4310	0.00808	0.345
Phenyl iodide	C_6H_5I	204.0	15/	1.64	124.4	44.6* calc.	5550	0.00739	0.327
Phenetole	$C_8H_{10}O$	122.1	15/	0.973	125.5	33.8	4240	0.00876	0.296
Dimethylaniline	$C_8H_{11}N$	121.1	20/	0.9575	126.5	35.8	4530	0.00879	0.315
Diisopropyl	C_6H_{14}	86.1	17.5/	0.6701	128.3	30.7*	3940	0.00744	0.228
Methyl valerate	$C_6H_{12}O_2$	116.1	17/	0.895	129.7	31.5	4090	0.00824	0.259
Ethyl butyrate	$C_6H_{12}O_2$	116.1	20/	0.8892	130.6	30.2	3940	0.00857	0.259
Amylformate	$C_6H_{12}O_2$	116.1	20/	0.8802	131.9	34.1	4500	0.00772	0.263

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Table II. (Continued).

Substance.	Formula.	M.	*t.*	ρ.	$\frac{M}{\rho}$.	π.	$\pi\frac{M}{\rho}$.	*b.*	πb.
Isobutyl acetate	$C_6H_{12}O_2$	116.1	16/	0.879	132.1	31.4	4190	0.00818	0.260
Diphenyl	$C_{12}H_{10}$	154.1	....	1.160	132.8	31.8	4220	0.0107	0.352
Ethyl isobutyrate	$C_6H_{12}O_2$	116.1	18.8/	0.871	133.3	30.1	4010	0.00841	0.253
Dipropylamine	$C_6H_{15}N$	101.1	0/	0.756	133.6	31.0	4140	0.00812	0.252
Pseudocumene	C_9H_{12}	120.1	0/	0.8901	134.9	33.2	4480	0.00902	0.299
Triethylamine	$C_6H_{15}N$	101.2	15/	0.735	137.6	30.0	4130	0.00818	0.245
Propylbenzene	C_9H_{12}	120.1	17/	0.8692	138.2	32.3	4460	0.00905	0.291
Isopropylbenzene	C_9H_{12}	120.1	17.5/	0.8658	138.7	32.2	4470	0.00904	0.291
Mesitylene	C_9H_{12}	120.1	13/	0.863	139.2	33.2	4620	0.00884	0.284
Dimethyl-*o*-toluidine	$C_9H_{13}N$	135.1	....	0.9324	145.1	30.8	4460	0.00993	0.306
Isobutylbenzene	$C_{10}H_{14}$	134.1	16/	0.8577	156.3	31.1	4860	0.00957	0.298
Cymene	$C_{10}H_{14}$	134.1	20/	0.8574	156.4	28.6	4470	0.01043	0.297
Octane	C_8H_{18}	114.1	17/	0.7032	162.3	24.6*	3990	0.01057	0.260
Diisobutyl	C_8H_{18}	114.1	18/	0.6940	164.4	24.5*	4030	0.01025	0.251
Isobutylisobutyrate	$C_8H_{16}O_2$	144.1	0/4	0.8750	164.7	....	....	.....	.....
Diphenylmethane	$C_{13}H_{12}$	168.1	26/4	1.0008	167.3	28.2	4720	0.01000	0.282
Decane	$C_{10}H_{22}$	142.2	15/	0.7342	193.6	21.0	4070	0.0130	0.273

Table III.

Substance.	$\pi\frac{M}{\rho}$.	Deviation from the mean.	Percentage deviation.
Methyl formate	[3460]		
Propyl alcohol	3750	—170	—4.3
Ethyl formate	3830	— 90	—2.3
Methyl acetate	3890	— 30	—0.8
Benzene	4200	+280	+7.1
Phenyl fluoride	4240	+320	+8.2
Propyl formate	4170	+250	+6.4
Ethyl acetate	3720	—200	—5.1
Methyl propionate	3890	— 30	—0.8
Methyl isobutyrate	3740	— 80	—2.0
Methyl butyrate	3810	—110	—2.8
Propyl acetate	3740	—180	—2.8
Stannic chloride	4240	+300	+7.6
Isopentane	3790	—130	—3.3
Ethyl propionate	3810	—110	—2.8
Hexane	[4590]		
Phenyl iodide (calculated)	[5550]		
Diisopropyl	3940	+ 20	+0.5
Octane	3990	+ 70	+1.7
Diisobutyl	4030	+110	+2.8
Mean value,	3920		3.7

tion. Further evidence in support of this view will be given later in the present paper.

Solubility and Molecular Volume.

If we consider that 2 substances of large molecular volume and, therefore, of small molecular attraction, as for example, ether and carbon tetrachloride, be brought into the presence of each other, it is easy to see that there is a greater chance of their being miscible than if we substitute one of them by a substance of small molecular volume and, therefore, of greater molecular attraction as, for example, water. For since neither the ether nor the carbon tetrachloride has strong internal attraction, a small force between them would cause them to mix, but with the water, on the contrary, whose internal attraction is very great, it might require quite considerable forces

between it and, say, carbon tetrachloride, to cause them to mix completely.

If we regard molecular attraction from a merely physical point of view, we must regard it as a mutual action between a particle and its fellows, as measured by the inverse molecular volume. Therefore, the part played by a single particle is proportional to the square root of this amount, and 2 dissimilar particles will attract each other with a force which is proportional to the product of their single attractions. Consequently, no 2 substances would be miscible whose molecular volumes were different by an appreciable extent. There is, however, a certainty that in many cases forces exist between dissimilar molecules which are not of the mere physical nature referred to above. Since these forces give rise to chemical reaction, it is customary to speak of them as chemical forces, but a reaction does not necessarily take place at once in the presence of these forces. Many reactions take place with appreciable velocity only in the presence of a catalyzer. The tendency of such forces would be to neutralize differences of molecular attraction between 2 substances, therefore, the number of mixtures would be increased. If, however, the molecular attraction of one of the substances is very great, as in the case of water, there would be less probability of its mixing with either ether or carbon tetrachloride, because the attractions between the unlike particles would then need to be rather large to overcome the effect of their very different molecular volumes.

It is evident that the views here expressed may be tested by experiment with great ease.

First of all let us refer to a solubility list due to Rothmund,[1] the substances being given in colume I. of Table IV. It represents the order of solubility of different classes of substances in water. He pointed out that the substances at each end of the list are miscible with each other, but that the solubility of the pairs decreases as the distance on the list between the components increases. This is in harmony with

[1] *Loc. cit.*

Table IV.

I. Rothmund's solubility list.	II. Type chosen.	III. Mol. vol.	IV.
Water	Water	18.0	1
Low acids	Formic acid	37.7	2
Low alcohols	Methyl alcohol	39.5	3
Low ketones	Acetone	72.5	7x
Low aldehydes	Acetaldehyde	55.6	4
Nitriles	Propionitrile	68.8	6
Phenols	Phenol	90.0	8
Arom. aldehydes	Benzaldehyde	100.9	10
Ether	Ether	103.0	11
Halogen derivatives	Carbon tetrachloride	97.1	9x
Carbon disulphide	Carbon disulphide	58.9	5x
Hydrocarbons	Hexane	129.9	12

my view of the nature of solubility; but we may go further and test the relation of the molecular volumes of the substances representing these classes. I attach importance to the above list because it was compiled by another worker who may be considered unprejudiced as far as this present theory is concerned. The substances representing his classes are given in colume II., their molecular volumes in column III. By the numerals in column IV. it is seen that the order of the molecular volumes agrees with the solubility order given by Rothmund in all except 3 cases. The chance of such a coincidence is less than 1 in 8,000,000.

Rothmund pointed out that there is a relation between the order of his solubility list and the dielectric constants of the substances representing those classes, but he was unable to explain the connection. If my theory is correct, the connection is not surprising, because dielectric constants are also connected with molecular volume.

My first paper on this subject[1] furnished a considerable amount of evidence bearing on the theory here given. That evidence is not conclusive, but it at least indicates a relation between molecular volume and solubility.

That work serves also to eliminate certain factors; for example, it is noticed that substances with a comparatively

[1] This Journal, **37**, 549 (1907).

high melting point, such as benzoic acid, do not behave abnormally on that account. Benzoic acid appears to behave almost exactly the same as phenyl chloride, whose molecular volume is nearly the same.

Rothmund thought of solubility as selective according to classes of compounds, that all alcohols are soluble in ethyl alcohol and all acids are soluble in acetic acid. We have found formic acid immiscible with oleic acid below 135° and miscible with substances as widely different as isoamyl alcohol and toluene. Hence, just as the molecular volume increases for all classes as we ascend the series, so the solubility appears to decrease.

When substances differ greatly in specific gravity, gravitation would tend to prevent solution. It was for this reason that the author worked with methylene iodide, sp. gr. = 3.285 at 15°. It is miscible with substances of nearly the same molecular volume, but becomes immiscible more quickly than the other compounds do. This may prove that the effect of gravitation upon solubility is appreciable. Further study will be devoted to this and other cases of a similar kind.

These experiments can only be regarded as preliminary, but they are of such a character as to warrant the further prosecution of the work. I have tried to give the theory as good a theoretical basis as possible, but it can only be accepted so long as it accounts for the known facts. It is seen that there are a great many interesting ways in which it may be further tested.

Conclusions.

1. Theoretical considerations seem to show that miscibility is dependent upon the attractions between the particles. The conditions for a critical solution temperature have been given.

2. The critical solution temperature is strictly analogous to the ordinary critical temperature when a foreign gas is present. A solution of a *liquid in a liquid* has been shown to pass imperceptibly into that of a *gas in a liquid*, and of a *gas in a gas*.

3. An explanation of the lower critical solution temperature has been offered and evidence brought forward to support that view.

4. Evidence has been given to show that molecular attractions are inversely proportional to molecular volumes.

5. It has been pointed out that the critical pressure is a measure of the molecular attractions at the critical temperature, and the product of critical pressure and molecular volume is a constant.

RICHMOND COLLEGE,
RICHMOND, VA.,
January, 1907.

REVIEWS.

A HISTORY OF CHEMISTRY FROM EARLIEST TIMES TO THE PRESENT DAY, being also an Introduction to the Study of the Science. By ERNST VON MEYER, PH.D., Professor of Chemistry in the Technical High School, Dresden. Translated with the Author's Sanction by GEORGE McGOWAN, PH.D. Third English Edition, translated from the Third German Edition, with various additions and alterations. London and New York: Macmillan Co. 1906. pp. 691. Price, $2.50 net.

A thorough review of the first edition of this book, written by Remsen, appeared in 1889.[1] A notice of the English translation appeared in 1891.[2]

This history has won a high place in the esteem of chemists. Several shorter works covering the same ground have appeared since the first edition of v. Meyer, but, thus far, nothing has been published which has won the same position, and it may be considered the best of the larger readable histories of chemistry.

It should not be forgotten that all later histories draw most of their material, except that for later years, from the mass heaped up by the labor of Kopp, and preserved in his "Geschichte der Chemie" and his "Entwicklung der Chemie in neuerer Zeit." Kopp's valuable books, however, owing to his singularly involved style, are extremely difficult reading for Germans, and repelling to a foreigner. To this fact, indeed, v. Meyer's book owed its ready acceptance at home and abroad.

In the arrangement of v. Meyer's book about two-thirds of the volume is given to the general development of the science from the earliest times to the present day. The remainder is special history of the various branches of chemistry during

[1] THIS JOURNAL, **11**, 429.
[2] *Ibid.*, **13**, 506.

the period after the time of Lavoisier. Since the publication of the second edition, the historical monographs of Kahlbaum and of Guareschi, the historical essays of Thorpe, and the books of Berthelot on the early history of chemistry have appeared, and the author acknowledges his indebtedness to these writers for material for revision of the book. The author has rewritten the history of the later years and added to it a careful study of the progress made during the last decade.

While a certain German bias is occasionally noticeable, v. Meyer is, on the whole, impartial, and gives space and credit to the work of chemists, in proportion to its importance, irrespective of nationality.

The book contains 70 pages more than the first edition. In its new form it will, doubtless, be welcomed by old readers and by new. E. R.

CONTRIBUTIONS FROM THE RESEARCH LABORATORY OF PHYSICAL CHEMISTRY OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 14. A System of Qualitative Analysis for the Common Elements. By ARTHUR A. NOYES and WILLIAM C. BRAY. Introduction, Outline of the Investigation. Part I., Preparation of the Solution. Part II., Analysis of the Silver, Copper and Tin Groups. Reprinted from the Technology Quarterly, Vol. XIX., No. 3, September, 1906.

The authors have undertaken an investigation for the purpose of studying and improving the methods used in qualitative analysis. They aim "to develop a system which will allow the detection of 1 or 2 milligrams of an element in any mixture" and "to employ only such processes as enable a rough estimate to be made of the quantity of the various elements present." "To this end tests of excessive delicacy like color reactions will be avoided, and each element obtained in the solid form as a precipitate or residue as far as possible."

The authors present the results of their investigation "in parts, each of which treats of a large division of the subject." Under each part is first presented a "General Discussion," in which are given the reasons for the adoption of the process employed. This is followed by a "Tabular Outline," which gives a survey of the important steps and the chemical reactions involved in the process of analysis. Then comes the chapter entitled "Procedures and Notes," in which the details of the process are presented and discussed. Next are given "Test Analyses".....finally "Confirmatory Experiments and References."

Part I. deals with the preparation of the solution. All preliminary tests are rejected, excepting the test for organic matter and water, by heating the substance in a closed tube.

Solvents are used in the following order: Water, nitric acid, hydrochloric acid, aqua regia. An insoluble residue is treated with hydrofluoric and sulphuric acids.

Part II. deals with the analysis of the silver, copper and tin groups. The authors retain the usual methods of precipitation and analysis of the silver group. "In the direction for the precipitation of the copper and tin groups by H_2S, special attention is given to securing the proper conditions as to acid concentration and temperature for a satisfactory separation of these elements from those of the iron group."

In the copper group the metals are separated in the usual manner, using the reaction of sodium stannite or bismuthyl hydroxide for final detection of bismuth, and separating cadmium from copper by precipitation as sulphide from the solution of potassium cuprocyanide and potassium cadmic cyanide.

While there is nothing new in the general methods of solution and analysis thus far, the details of treatment are improved and made accurate.

In the analysis of the tin group, the authors give us a new and most accurate method of separating arsenic, antimony and tin. It depends on the solubility of arsenic sulphide, antimonic sulphide and stannic sulphide in hydrochloric acid of different concentrations. The arsenic sulphide is separated as usual by its insolubility in a measured volume of hydrochloric acid of 1.20 sp. gr. at about 100°, the filtrate is diluted with a certain measured volume of water, and at 90° hydrogen sulphide precipitates all antimony as pentasulphide, Sb_2S_5. The filtrate from this is diluted with a certain volume of water; hydrogen sulphide precipitates stannic sulphide, SnS_2.

The reviewer has tried the method with undergraduate students making their first attempt in the analysis of this group, and found that, without exception, they obtained very satisfactory results in the same time that other beginners required to analyze the group by the usual methods with less reliable result; the students also readily separated tin from antimony by this method when so little of one of these elements was present that separation by the common method gave a doubtful result.

The educational value of a qualitative method requiring measured strength and volume of reagent, measured temperature and measured time of reaction, is very great, and such methods form the best preparation for quantitative work.

In addition to the common metals the separations of platinum, selenium, tellurium and molybdenum are included in this scheme.

Wherever the application of the theory of electrolytic dissociation, or the law of mass action would assist in making the reactions clear, the authors make such application.

Teachers of analytical chemistry owe much to Noyes and Bray for their thorough investigation, and will eagerly await the completion of the system.

E. RENOUF.

PHOTOGRAPHY FOR STUDENTS OF PHYSICS AND CHEMISTRY. By LOUIS DERR. London and New York: Macmillan Co. 1906. Price, $1.40 net.

This little book occupies a place midway between the dealer's handbook, telling how to go through photographic manipulations, and the detailed treatise, monographs on special topics, and the like, intended for the specialist in scientific photography. It is planned, as the author explains, for students who, using photography in their physical and chemical work, are interested enough in the processes gone through to wish to learn something of the underlying science. Such a book should, above all, be clear and interesting. This desideratum is well fulfilled in the present case, the numerous excellent illustrations assisting materially thereto.

The first chapters are occupied with a consideration of the camera and its accessories. The lens is treated at considerable length, starting with the simplest image-forming device, the pin-hole. Of particular use to the physicist or chemist who desires to do photographic work should be the chapter on the various classes and makes of lenses, from which he may learn what he needs, and, often of more importance, what he does not need, in the way of a lens. Aberrations, astigmatism, distortion, and similar faults, are defined, explained, and the methods of detection satisfactorily outlined. The explanation of camera perspective in the chapter on diaphragms would, perhaps, be more effective were an illustration inserted, instead of the mere mention that a 6-inch fish can be made to assume imposing proportions if photographed with its captor in the proper, or perhaps one should say, improper fashion.

Of more direct interest to the student of chemistry, probably, is the second portion of the book. In this the photographic plate is considered, the chemistry of exposure, development, fixing, washing, intensification and reduction. The question of gradation rendering both in the normally exposed plate and as affected by intensification and reduction is given the emphasis it deserves. Chapters on halation, reversal, and markings on the plate add to the usefulness of the work as a guide to correct manipulation.

Two chapters are devoted to lantern slides and printing processes. It is to be regretted that more attention could not have been given to other applications of photography of which the student is likely to have need. A chapter on photomicrography and photographing with optical instruments in general would be a desirable feature. Also a chapter on the several extremely interesting photo-mechanical reproduction processes could well find a place here.

The last chapter is on color photography. Of this interesting subject the author gives merely the main outlines of the principal direct and indirect methods. Doubtless the small opportunity afforded the average student at present for trying his hand at these processes calls for no more than this brief treatment. One error is to be noted in the account of the three-color process. Everywhere the pictures are spoken of as being taken through "red, green and violet" glasses, and viewed by the same colors. The correct account of the essential difference between the "taking screens," which between them transmit all the spectrum colors, and the "viewing screens," which are monochromatic, in view of the very general misconception regarding these special facts, should have been emphasized, and this could easily have been done. Several other statements in the book dealing with color cannot be taken quite literally; for instance, calling the color of the spectrum at C "orange-red" looks well on paper as fitting neatly in the gap between "B-red" and "D-yellow," but does not find support in the deep unmistakable red of that line as seen by the normal eye.

Aside from these slight errors and omissions, the latter, of course, being largely a matter of personal opinion, this book contains an immense amount of interesting and useful information. It should be an excellent addition to the student's library.

H. E. Ives.

Inorganic Qualitative Chemical Analysis for Advanced Schools and Colleges. By William Stowell Leavenworth, M.Sc., Professor of Chemistry, Olivet College. Easton, Pa.: Chemical Publishing Co. 1906. pp. 153. Price, $1.50.

The author says that he "aims to offer a manual which will occupy an intermediate position between the elaborate treatise and the skeleton outline."

The only feature in which this differs from certain other similar books is the method of putting questions to the student in the text, used by Remsen and his followers in text-books and applied to qualitative analysis many years ago by Volhard.

The methods of separation are good and the book, doubtless, gives satisfaction. E. R.

THE TOXINS AND ANTI-TOXINS AND THEIR ANTI-BODIES. By EM. POZZI-ESCOT. Authorized translation by ALFRED I. COHN, PHAR.D. New York: John Wiley & Sons. 1906. Price, $1.00 net.

The booklet of 100 pages before us cannot be viewed as a very successful effort to present, in brief space, a simple and substantial account of the subject-matter given in the title. It deals, indeed, with a wide series of substances from leucomaines and ptomaines to the poisons (toxins?) of certain animals and insects, many of which have hardly any scientific standing at all. The account of the toxins and anti-toxins proper is brief and scarcely adequate to their understanding, or their present importance among the various bodies described in the book. The subject of the toxins and anti-toxins is one that must present, at this time, almost insuperable difficulties to any one attempting a popular exposition. Chemists have not arrived, as yet, at any decision as to their nature; and the biological phenomena upon which their actions, recognitions and properties chiefly depend are exceedingly complex and only slightly understood. The hypotheses of Metschnikoff, Ehrlich and others through which attempts have been made to grasp the meaning of the anti-bodies, immunity to micro parasites and their poisons, brilliant as they are, cannot be presented in a few brief paragraphs in such a manner as to be intelligible to the casual reader. The consideration given the phenomenon of phagocytosis would not enable the unprofessional reader to form any conception of the nature of this fundamental process; and the references to Ehrlich's side-chain theory of immunity, etc., must be, even to chemists, accustomed to think in the terms of the more definite chemical conception, as opposed to the more fanciful morphological one, little enlightening. The influence of the French school on the author's convictions is found in the stress laid upon the diastatic nature of the toxins. One could hardly imagine, from the prominence given this conception, that it is based upon circumstantial evidence which to many scientists is wholly unconvincing. The translator has, apparently, done his work well for the most part; but whether to him or to the author is to be discredited the statement made once or twice that Ehrlich's theory furnishes us with an explanation of the formation of anti-toxins in tumors, it would be interesting to know.

There is a dearth of semi-popular books dealing with the important subject of toxins, anti-bodies, immunity, and re-

lated phenomena. It may even be hazarded that the time is still unripe for the appearance of such a work which would be adequate in its treatment. The present volume fails to meet the requirements of such a volume. S. F.

BOILER-WATERS. SCALE, CORROSION AND FOAMING. By WILLIAM WALLACE CHRISTIE. New York: D. Van Nostrand Co. 1906. pp. vii + 235. Price, $3.00 net.

The importance of this subject in connection with steam-making has long been recognized by Master Mechanics, but only within comparatively recent years has proper attention been devoted to it by those most concerned. This book is intended to "furnish steam users with information regarding water, its use, the troubles arising from the use and remedies that may be used." There are 10 chapters covering the different subjects treated. There appears to be some lack of co-ordination in different parts of the book, and the reader is left somewhat uncertain as to the conclusions: Thus, on p. 41, we read, from Stromeyer and Baron, "Scale does not materially reduce the efficiency of a boiler, but it seriously increases its wear and tear," etc. But on p. 53, experiments by Hirsch show that scale 0.2 inch thick caused an increase of 460° in temperature on the fire side, to evaporate 55 lbs. of water per hour. And thus scale offers five times the resistance to the transmission of heat that iron does. And on p. 57, Bell is quoted to the effect that a slightly scaled boiler evaporated 8.04 lbs. water per lb. of dry coal, while the same boiler, when clean, evaporated 10.3 lbs. per lb. of coal. And on p. 58 is a table showing the losses of conductivity of heat due to scale; and on p. 59, as the results of tests on a locomotive, a loss of 9.55 per cent is ascribed to a scale 3/64 inch in thickness. The character of the scale has great effect upon the quantity of heat loss.

In the chapter on Priming and Foaming, a clear distinction is not made between the two phenomena, and under the heading of Priming there appears a considerable amount of information about Foaming. The author quotes Koyl as attributing foaming to the presence of finely divided sediment in the water and discredits the effects of free alkali as the producer of foam.

Some typographical errors may be noted for future correction. On p. 8, line 10 from the bottom, calcium sulphate appears where sodium sulphate was probably intended; on p. 14, the unqualified statement is made that aluminum oxide is insoluble in acids and soluble in water. In the table of symbols, misprints in the formula for iron rust, potassium

bicarbonate, kaolin, boric acid and talc, have been noted. These defects have not been specified in any spirit of unreasonable criticism, but as an aid to the production of the more perfect work which the author promises in the near future.

The chapters on Feed-water Heaters is well presented and copiously illustrated, a number of standard makes being described. The chemistry of water softening is very well treated in Chap. IX., and descriptions of a number of appliances for carrying on the processes are included. The chapters on Corrosion and Oil contain much information with which every steam user and engineer in charge of boilers should be made acquainted. The typographic work and general make up of the book is very good and the illustrations are excellent.

F. H. T.

PHYSICAL CHEMISTRY IN THE SERVICE OF MEDICINE. Seven Addresses by Dr. WOLFGANG PAULI, Privatdocent in Internal Medicine at the University of Vienna. Authorized translation by DR. MARTIN H. FISCHER, Professor of Pathology at the Oakland College of Medicine. First Edition. New York: John Wiley & Sons. 1907. pp. 156. Price, $1.25 net.

This small volume contains the translations of 7 addresses by the Viennese investigator whose name has become known through his excellent work on the action of salts on proteids. The author states that the volume is to be looked upon as a modest attempt to win friends capable of working in this fruitful field of labor.

In the course of the addresses the author discusses the following principal topics: "The Colloidal State and the Reactions that Go On in Living Matter;" "Therapeutic Studies on Ions" and "The Relation of Physico-chemical Properties and Medicinal Effects;" "Changes Wrought in Pathology through Advances in Physical Chemistry."

It is perfectly obvious that the author is a great enthusiast in this particular field of work, in consequence of which the book is very interesting. No one can doubt the great service of an enthusiast in a certain field even if he ignores other branches which should be taken into consideration. It is difficult to criticize a book of this character and at the same time to avoid giving the impression of being antagonistic to the line of work in question. It is perfectly apparent, even to the casual observer, that a clearer understanding of the colloidal state and the action of salts on proteids is of prime importance to all of the biological sciences and the reviewer is in entire sympathy with attempts to use all physiochemical methods available for the elucidation of these problems. However, the one-sidedness of the writer's point of view detracts very much

from the value of the book and, in places, gives rise to antagonism even in those in sympathy with the work. Thus, in the address entitled, "Therapeutic Studies on Ions" the author quotes certain experiments on the precipitating action of salts upon proteid, from which he concluded that sulphocyanates should possess pharmacological properties similar to the iodides. He does not mention here what proteid he used. He then proceeded to test his views by administering these substances to patients. The clinical results presented are of absolutely no value as corroborative evidence. In the table given, the fluorides stand next to the sulphates and, reasoning similarly, they should have similar pharmacological effects yet they could hardly be further apart. In speaking of the analogy between changes in the organic colloids and life phenomena, the author makes the following statement: "Besides a limited identity, extensive differences may therefore exist, many of which are still beyond our understanding." This sentence illustrates the general theme of the addresses. It has been known for some years that the effect of a certain series of salts on gelatin, when arranged in the order of their action, will be found to stand in the same order in certain of their pharmacological effects. This parallelism has been carried too far by the author, as is indicated by the phrase "limited identity" in the above quotation instead of the word "similarity." The author seems to consider the chemistry of a salt exhausted so far as its pharmacological action is concerned when its precipitating action on certain laboratory preparations of the proteids has been studied.

A few omissions of recent work occur. Thus, on p. 59, the author states that the unit of molecular concentration of a non-dissociable substance is the molecular weight expressed in grams, dissolved in enough water to make a liter. Morse and Frazer have shown that a liter of the solvent must be used regardless of the total volume of the solution and it is important that this fact should speedily find its way into biological literature on these subjects.

The work of the translator is fairly satisfactory, but in many places the sentences have the typical German construction. The book presents an interesting summary of this line of work, the value of which is somewhat lessened by the absence of references to the literature. A. S. L.